ETIOLOGICAL, CLINICAL PROFILE AND OUTCOME IN ADULTS WITH MENINGITIS AND MENINGOENCEPHALITIS

Dissertation submitted to

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY, CHENNAI

In fulfilment of the regulations for the award of the degree of

Doctor of Medicine in General Medicine

DEPARTMENT OF GENERAL MEDICINE

P.S.G INSTITUTE OF MEDICAL SCIENCES & RESEARCH

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY,

CHENNAI, TAMIL NADU

APRIL 2016

ETIOLOGICAL, CLINICAL PROFILE AND OUTCOME IN ADULTS WITH MENINGITIS AND MENINGOENCEPHALITIS

Dissertation submitted to

The Tamil Nadu Dr. M.G.R Medical university, Chennai

In fulfilment of the requirements for the award of the degree of

Doctor of Medicine in General Medicine

Under the guidance of

PROFESSOR. JAYACHANDRAN .K, M.D.,

DEPARTMENT OF GENERAL MEDICINE

P.S.G INSTITUTE OF MEDICAL SCIENCES & RESEARCH, COIMBATORE

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY,

CHENNAI, TAMIL NADU

APRIL 2016

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled, **"ETIOLOGICAL, CLINICAL PROFILE AND OUTCOME IN ADULTS WITH MENINGITIS AND MENINGOENCEPHALITIS"** is the bonafide original work of **Dr. DIVYA PEDDIREDDY** in fulfilment of the requirements for the degree of Doctor of Medicine in General Medicine.

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ENDORSEMENT BY THE HOD, DEAN OF THE INSTITUTION

This is to certify that the dissertation entitled, **"ETIOLOGICAL, CLINICAL PROFILE AND OUTCOME IN ADULTS WITH MENINGITIS AND MENINGOENCEPHALITIS"** is the bonafide original research work of **Dr. DIVYA PEDDIREDDY** under the guidance of **Dr JAYACHANDRAN.K, M.D.**, Professor of Medicine, PSG IMS&R, Coimbatore in partial fulfilment of the requirements for the degree of Doctor of Medicine in General Medicine.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled "**ETIOLOGICAL, CLINICAL PROFILE AND OUTCOME IN ADULTS WITH MENINGITIS AND MENINGOENCEPHALITIS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. JAYACHANDRAN .K, M.D.,** Professor of Medicine, PSG IMS&R, Coimbatore.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University in fulfilment of the University regulations for the award of MD degree in General Medicine. This dissertation has not been submitted for award of any other degree or diploma.

Signature of the Candidate

Dr. DIVYA PEDDIREDDY

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June 18, 2014

To
Dr Divya Peddireddy
Postgraduate
Department of General Medicine
PSG IMS & R
Coimbatore

Ref.: Proposal titled: *"Etiological, clinical profile and outcome in adults with meningitis and meningoencephalitis"*

Sub.: Ethics Committee Approval for the study

The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on 16th June, 2014 in its full board review meeting held at Research Conference Room, PSG IMS&R, between 9.30 am and 12.30 pm, and discussed your application to conduct the study entitled:

"Etiological, clinical profile and outcome in adults with meningitis and meningoencephalitis"

The following documents were received for review:

1. Duly filled application form
2. Proposal
3. Informed Consent forms
4. Data Collection Tool
5. Permission letter from the concerned Head of Department
6. CV
7. Budget

The members who attended the meeting at which your study proposal was discussed are as follows:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
2	Mrs. Geetha S Kannan	+ 2	Lay person	Female	No	Yes
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5	Mr. R. Nandakumar (Vice-Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
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10	Dr. Seetha Panicker	MD	Clinician (Obstetrics & Gyanaecology)	Female	Yes	Yes
11	Dr. S. Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
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14	Mrs. K. Uma Maheswari	M Sc, M Phil. B Ed	Botany	Female	No	No
15	Dr. D. Vijaya	M Sc, Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

After due consideration, the committee has decided to approve the above proposal.

The approval is valid for one year.

We request you to intimate the date of initiation of the study to IHEC, PSG IMS&R and also, after completion of the project, please submit completion report to IHEC.

We hereby confirm that neither you nor any of your study team members have participated in the voting/ decision making procedure of the committee. The members of the committee who have participated in the voting/ decision making procedure of the committee do not have any conflict of interest in the referenced study.

This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

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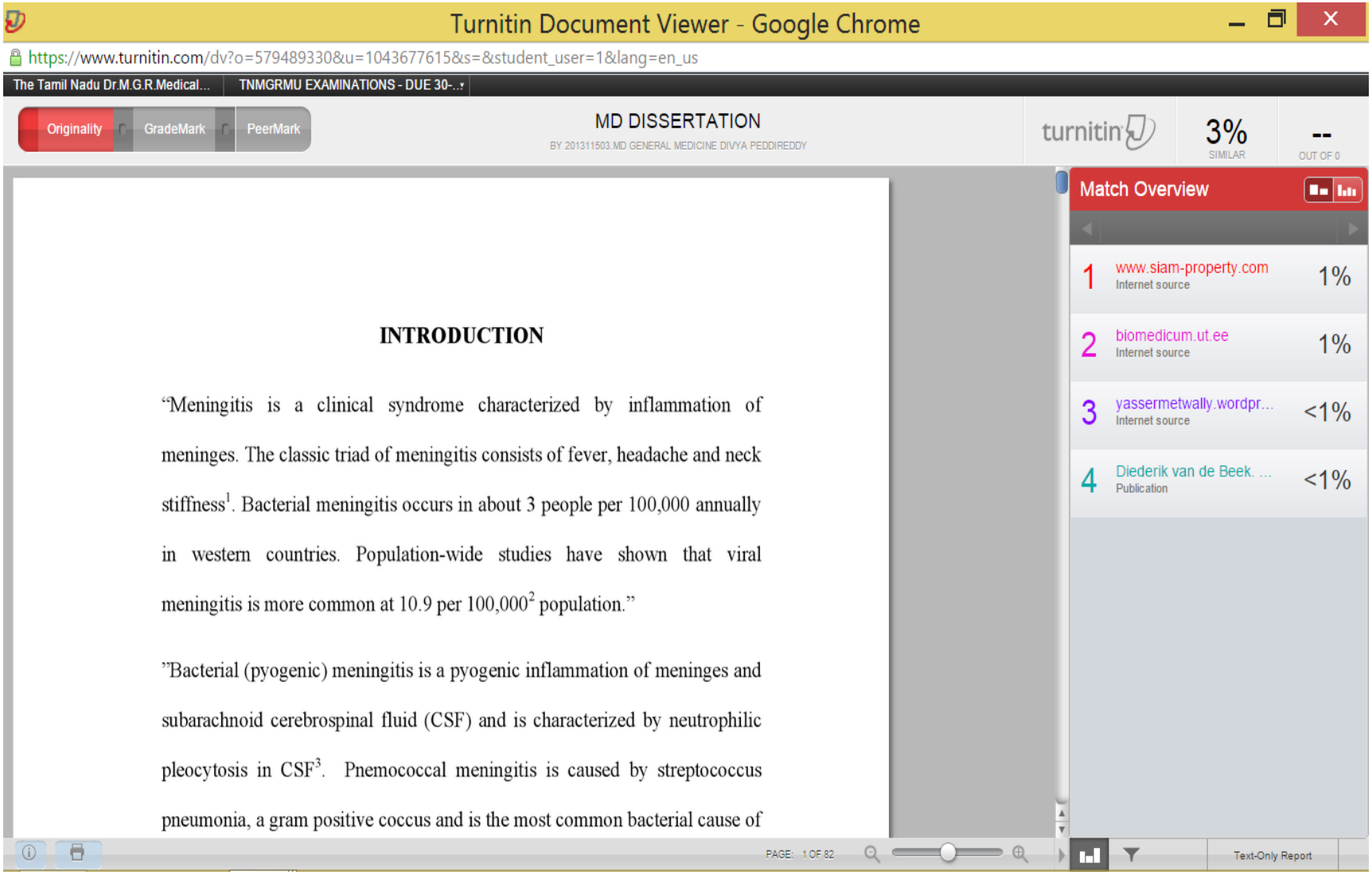
Proposal No. 14/193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INTRODUCTION
"Meningitis is a clinical syndrome characterized by inflammation of meninges. The classic triad of meningitis consists of fever, headache and neck stiffness[1]. Bacterial meningitis occurs in about 3 people per 100,000 annually in western countries. Population-wide studies have shown that viral meningitis is more common at 10.9 per 100,000[2] population."
"Bacterial (pyogenic) meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF[3]. Pnemococcal meningitis is caused by streptococcus pneumonia, a gram positive coccus and is the most common bacterial cause of
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CONTENTS

ABSTRACT

Introduction: Meningitis is a clinical syndrome characterized by inflammation of meninges. The classic triad of meningitis consists of fever, headache and neck stiffness. Pnemococcal meningitis is the most common bacterial cause of meningitis. Most patients recover completely if appropriate antibiotic therapy is instituted promptly. Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment. Death may occur as a result of missed diagnosis and delayed treatment. Enterovirus is the most common cause of viral meningitis. Cryptococcal meningitis may be seen especially in persons with defective cell mediated immunity. Encephalitis primarily involves the brain, it often involves the meninges as well (meningoencephalitis). There are no studies done till now showing the clinical, etiological profile and outcome in patients with meningitis and meningoencephalitis. There are some studies done in children but not in adults. Distinguishing the etiologies also helps in terms of both reducing antibiotic usage and hospital bed occupancy and reassuring contacts of cases and health care staff of a non-bacterial cause. As there are fewer developments in therapies for viral meningitis and there remain no effective therapies for most pathogens, this study is done to emphasise the importance of early diagnosis, so that prompt management is given at appropriate time.

Aim: To establish the cause and to identify the clinical differences between causes and outcome in adults with meningitis and meningoencephalitis in a tertiary care hospital.

Materials and methods: In the present study, we recruited 50 patients who presented with meningitis and meningoencephalitis who fulfilled the inclusion criteria. Proforma is used to collect data needed. Data are statistically analysed.

Results: Among the 50 patients 33(66%) are male patients. 39 patients (78%) were young adults(<50 age group).The common presenting symptoms are fever in 41 patients(82%), headache in 37 patients (74%), altered sensorium in 31 patients(62%). etiological diagnosis was tuberculous meningitis in 29 patients(58%), acute pyogenic meningitis in 8 patients (16%), viral meningitis in 8 patients(16%), others in 5 patients (10%). In terms of outcome 47 patients recovered completely.

Conclusion: In the present study we found that, most of the patients with meningoencephalitis were males and young adults. Surprisingly, tuberculous meningitis was the most common overall cause in our study. Both viral meningo encephalitis and pyogenic meningitis constituted most of the cases of acute Meningoencephalitis.

Tuberculous meningitis was the most common cause in patient with subacute meningitis. All patients with chronic presentation had tuberculous meningitis. We came across atypical presentation of cryptococcal meningitis in a non HIV patient.In this study, we are reporting an interesting case of aspergillus Meningitis which is a very rare entity especially without co-existent aspergilloma. 47 patients recovered well without neurological deficits.

Keywords: Meningitis, Meningoencephalitis, Pneumococci, Tubercular, Viral, Fungal.

INTRODUCTION

Meningitis is a clinical syndrome characterized by inflammation of meninges. The classic triad of meningitis consists of fever, headache and neck stiffness[1]. Bacterial meningitis occurs in about 3 people per 100,000 annually in western countries. Population-wide studies have shown that viral meningitis is more common at 10.9 per 100,000[2] population.

Bacterial (pyogenic) meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF[3]. Pnemococcal meningitis is caused by streptococcus pneumonia, a gram positive coccus and is the most common bacterial cause of meningitis. Meningococcal meningitis is caused by gram-negative diplococcus - Neiserria meningitides. Most patients recover completely if appropriate antibiotic therapy is instituted promptly[3].

Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment[4]. Tuberclous meningitis should be a strong consideration when a patient presents with clinical picture of meningoencephalitidis, especially in high risk groups, including persons with malnutrition, those with abuse alcohol or drugs and patients with known retroviral infection. Death may occur as a result of missed diagnosis and delayed treatment[5].

World-wide causes of viral meningitis include enterovirus, herpes, mumps, measles and HIV. Enterovirus is the most common cause of viral meningitis.

Aseptic meningitis is an illness characterized by serious inflammation of the meninges, usually with an accompanying CSF lymphocyte pleocytosis. Clinical manifestations vary with headache and fever predominating. The illness is usually mild and runs its course without treatment, however some cases can be severe and life threatening.

Remarkable recovery may be achieved in some patients with viral meningitis who become even comatosed. Vigorous supportive therapy and avoidance of complications are very important in managing these patients[6].

Cryptococcal meningitis is caused by the yeast Cryptococcus neoformans, especially in persons with defective cell mediated immunity. Prompt antifungal therapy should be considered in these patients[7].

The incidence of acute encephalitis in western countries is 7.4 per 100,000 population per year. In tropical countries like India it is 6.4 per 100,000 per year. Herpes simplex encephalitis has an incidence of 2-4 per million population per year.

Encephalitis presents as diffuse or focal neuropsychological dysfunction although it primarily involves the brain, it often involves the meninges as well (meningoencephalitis). From an epidemiologic and pathophysiologic perspective encephalitis is distinct from meningitis, though on clinical

evaluation both can be present, with signs and symptoms of meningeal inflammation. The prodome typically consists of fever, headache, nausea, vomiting, lethargy and myalgias.

The clinical presentation is encephalopathy with diffuse or focal neurological symptoms including behavioural and personality changes, with decreased level of consciousness, neck pain/stiffness, photophobia, lethargy, generalized or focal seizures, acute confusion or amnestic states and flaccid paralysis[8].

There are no studies done till now showing the clinical, etiological and outcome in patients with meningitis and meningoencephalitis. There are some studies done in children but not in adults.

Distinguishing the etiologies also helps in terms of both reducing antibiotic usage and hospital bed occupancy and reassuring contacts of cases and health care staff of a non-bacterial cause.

As there are fewer developments in therapies for viral meningitis and there remain no effective therapies for most pathogens, this study is done to emphasise the importance of early diagnosis, so that prompt management is given at appropriate time.

AIMS AND OBJECTIVES

- To establish the cause and to identify the clinical differences between causes and outcome in adults with meningitis and meningo encephalitis in a tertiary care hospital.

MATERIALS AND METHODOLOGY

Type of study: Prospective(observational) study

Place of study: PSG Hospitals, PSG IMS & R , Coimbatore.

Duration of Study: One year (June 2014 – June 2015)

Study Population:

Patients older than 18 years of age diagnosed with meningitis and meningoencephalitis of various etiologies admitted in Department of General Medicine and Neurology. Patient sample size is restricted to a total number of 50 cases.

Inclusion Criteria:

- Patients with community acquired meningitis
- Patients who underwent lumbar puncture for the diagnosis
- Patients with both positive and negative cerebrospinal fluid cultures.

Exclusion Criteria:

- Patients with hospital acquired meningitis
- Patients with neurosurgical devices
- patients with recent history of neurosurgery
- Myelitis

METHODOLOGY

The study is based on prospective collection of data of adults aged older than 18 years of age, admitted at PSG hospitals, Coimbatore diagnosed with meningitis and meningoencephalitis of various etiologies, confirmed with clinical features, laboratory investigations, and brain imaging and meeting the inclusion criteria as mentioned above, during the study period of June, 2014 to June, 2015 are taken into consideration for the study. A proforma is prepared which included detailed history, clinical examination and requisite investigations available in the hospital. After taking informed consent from the patient, history and clinical findings attributable to the meningitis and meningoencephalitis are collected in detail. Investigations like complete hemogram, routine urine analysis, blood sugar, serum electrolytes, serum creatinine, blood urea,liver function tests ,blood cultures, chest X-ray, electrocardiogram,CSF analysis(CSF sugar, protein, total count, differential count, gramstain, bacterial culture,Z.N stain for AFB, India ink stain for Cryptococcus, cryptococcal antigen test, automated culture for AFB, CT or MRI brain were done in all patients. Investigations like CSF PCR studies were done in the patients as required.

According to the patients duration of illness, patients were sub classified into acute, subacute and chronic. According to patients clinical presentation, duration of illness, CSF analysis and brain imaging findings, patients were classified according to their etiology.

Patients are examined clinically in detail and their severity is assessed based on the clinical grounds, laboratory investigations and brain imaging findings.

To assess the clinical outcome of the patients, the barthel index was used. Based on this index patients functional evaluation was done at the end of the first month.

The results were analysed to assess the clinical presentation, etiology, and clinical outcome in these patients diagnosed with meningitis and meningoencephalitis.

Statistical tools:

The data collected from the patients is tabulated using Microsoft Excel. The data are reported as the mean +/- SD or the median, depending on their distribution. The differences in quantitative variables between groups were assessed by means of the unpaired t test. Comparison between groups was made by the non-parametric Mann- Whitney test.

A Chi square test was used to assess differences in categoric variables between groups.A p value of <0.05 using two tailed test was taken as being of significance for all statistical tests. All data were analysed with a statistical software package (SSPS version 16.0 for windows)

REVIEW OF LITERATURE

Meningitis is defined as the inflammatory process of the membranes that surround the brain and spinal cord. Meningitis is also referred to as arachnoiditis or leptomeningitis. Meningitis affects the arachnoid, pia and CSF.

When the meninges, the subarachnoid space, and the brain parenchyma are all frequently involved in the inflammatory reaction it is defined as meningoencephalitis.

Meningitis was initially recognized in the early 1800's[9]. Even until the beginning of 20th century bacterial meningitis was nearly 90% fatal. This shows that the disease is most virulent and causes a great deal of mortality and morbidity. The advent of the antibiotics in the beginning of the twentieth century brought a cure to meningitis. Inspite of antibiotics the sequelae of meningitis after completion of treatment is a great burden to the society.

Meningitis can occur in any age group but the extremes of age group are the most dreadfully affected. The immunocompromised states also lead to a high mortality and morbidity. The overall case fatality rate of bacterial meningitis in adult patients is around 30%[10-12].

Moreover, in the emergency setting differentiating bacterial meningitis from other causes such as fungal, tubercular, viral, neoplastic, toxic or autoimmune causes is extremely difficult. If a diagnosis of meningitis is made, it is prudent

to start the patient on empirical antibiotics until the cultures and other results are awaited[13].

Bacterial meningitis is the most common suppurative CNS Infection. It is a medical emergency. Annual Incidence in United States is >2.5 cases/ 100,000 population. Organism responsible for bacterial meningitis are streptococcus pneumoniae (50%), Neisseria Meningitis (25%), group B streptococci (15%) & listeria monocyctogens (10%), heamophilus influenza type b (<10%)

The term aseptic meningitis is used for all types of inflammation of the brain meninges which is not caused by pus producing bacteria. It is usually a benign syndrome[14]. Although viruses are a major cause, many different etiologies both infective and non infective can cause aseptic meningitis. Hence the term is not synonymous with viral meningitis although the two are often used interchangeably.

Aseptic meningitis is one of the most common inflammatory disorders of the meninges. It occurs at all ages, although more common in children. No racial differences in occurrence have been reported. The incidence of aseptic meningitis in the US has been reported as 11 per 100,000 people - years, compared to 8.6 per 100,000 for bacterial meningitis[15]. The illness is responsible for 26,000 - 42,000 hospitalisations each year in the US[16]. A recent study in children from Singapore found an incidence of 37 cases per

10,000 hospital admissions[17]. Comparable figures for India are not available.

ETIOLOGY

S. pneumonia is the most common cause of bacterial meningitis in adults > 20 years of age, accounting for nearly half the reported cases (1.1 per 100,000 persons per year). The predisposing condition may include pneumococcal pneumonia, acute or chronic pneumococcal sinusitis or otitis media, CSF Rhinorrhea, head trauma with basilar skull fracture, alcoholics, diabetes, splenectomy, hypogammaglobulinemia and complement deficiency.

The Incidence of Meningitis due to N. Meningitis has reduced due to the routine immunization of 11 yr - 18 yr old with quadrivalent (serogroups A, C, W - 135 and y) meningococcal glycoconjugate vaccine. The vaccine does not contain serogroup B, which is responsible for one third of cases of meningococcal disease. Meningococcal infection may be initiated through nasopharyngeal colonization; the patient may be an asymptomatic carrier or may result in invasive disease. The risk of development of invasive disease depends on the bacterial virulence factors and host immune mechanism.

Gram negative bacilli infection can be suspected in patient with chronic and debilitating disease such as diabetes, cirrhosis, chronic urinary tract infection and alcoholism. Gram negative meningitis can also complicate neurosurgical

procedures, mainly craniotomy and head trauma associated with CSF Rhinorrhoea or otorrhoea.

Otitis, Mastoiditis, sinusisits are predisposing conditions for meningitis due to staphylococcus aureus, streptococci sp, Gram negative anaerobes, heamophilus sp and enterobacteriacea.

Meningitis complicating endocarditis may be due to viridans streptococci, S.aureus, HACEK group, enterococci or streptococcus bovis,.

Group B Streptococcus or streptococcus agalactiae is seen mostly in patients > 50 years of age and those with underlying disease.

L.Monocytogenes infection is suspected in patients with age > 60 years, immunocompromised patients, pregnant women. Infection is mainly obtained by ingesting contaminated foods.

H. influenza meningitis is suspected in children (who are unvaccinated with Hib conjugate vaccine) and older adult. Non - b H.influenza is also an important pathogen.

S.aureus and coagulase negative staphylococci meningitis is possible in patients following invasive neurological procedures.

Aseptic meningitis may be considered as a syndrome with many possible etiologies. Viral meningitis is the most common cause of aseptic meningitis.

Viral infections of the central nervous system may involve primarily the brain parenchyma, the meninges, the anterior horn cells,cranial nerves etc. When the infectious agent primarily attacks the brain parenchyma the clinical picture of 'encephalitis' with obtundation, seizures and coma is produced. When the inflammation is primarily of the meninges, a milder syndrome of viral or aseptic meningitis is produced.

Pathologically and clinically there is a continuum between the two and some degree of meningeal inflammation is found with encephalitis and vice versa. Therefore the term viral meningoencephalitis appears more appropriate. Most of these viruses characteristically cause either an 'encephalitic' or 'meningitic' picture. However, it must be borne in mind that the same agent may cause a very wide range of severity and occasionally produce an atypical illness.

Etiology of Meningitis

Infectious Causes

1. Viruses:

- Enteroviruses - polio, coxsackie, ECHO virus
- Herpes Group of viruses
- Herpes Simplex virus type 1 and 2
- Varicella zoster virus
- Cytomegalovirus

- Ebstein Barr virus
- Human herpesvirus 6 (HHV-6)
- Respiratory viruses
    - Adenovirus
    - Rhino virus
    - Influenza virus type A & B
- Arboviruses
- Mumps virus
- Lymphocytic choreomeningitis
- HIV

2. Bacteria:

- Streptococcus pneumoniae
- Neisseria Meningitis
- Group B streptococci
- Listeria monocyctogens
- Heamophilus influenza type b
- Parameningeal infection
- Endocarditis
- Mycoplasma pneumoniae
- M tuberculosis
    - Ehrlichiosis

- Borrelia burgdorfi
- Treponema pallidum
- Brucella
- Leptospirosis

3. Fungi

- Cryptococcus neoformans
- Histoplasma capsulatum
- Coccidiodes immitis
- Blastomyces dermatitides
- Candida

4. Parasites

- Toxoplasma gondii
- Neurocysticercosis
- Trichinosis
- Naeglaria
- Hartmenella
- Bartonella henselae

5. Rickettsiae

- Rocky mountain spotted fever
- Typhus

II Non infectious Causes

1. Post infectious, post vaccinial

- Rubeola
- Rubella
- Varicella
- Variola
- Rabies vaccine
- Pertussis vaccine
- Influenza vaccine
- Vaccinia
- Yellow fever vaccine

2. Drugs

- Non steroidal anti-inflammatory drugs (NSAIDs)
- Trimethoprim sulfamethoxazole, amoxicillin
- Muromonab CD3 *(OKT3)*
- Azathioprine
- Intravenous immunoglobulin
- Isoniazid
- Intrathecal methotrexate
- Intrathecal cytosine arabinoside

- Allopurinol
- Carbamazepine
- Sulfasalazine

3. Systemic Disease

- Collagen vascular disorders
- Systemic lupus erythematosis
- Wegener granulomatosis
- Central nervous system vasculitis
- Rheumatoid arthritis
- Kawasaki's disease
- Sarcoidosis
- Leptomeningeal cancer
- Post transplantation lymphoproliferative disorder
- Behcet disease
- Vogt- Koyanagi syndrome

4. Neoplastic disorders

- Leukemia
- Carcinomatous meningitis secondary to primary or secondary tumours of the brain

5. Inflammation of neighbouring structures

- Brain abscess
- Epidural abscess

6. Miscellaneous

- Arachnoiditis
- Migraine
- Urinary tract infection

The most common viruses causing aseptic meningitis are the enteroviruses[18], which account for more than half the cases. More than 50 serotypes have been linked with meningitis.

Mumps is another important cause of viral meningitis. Herpes viruses both type 1 (herpes labialis) and type 2 (genital herpes) can cause meningitis in children, especially infants. Varicella zoster virus can also cause meningitis but only in those who are immunocompromised. HIV may cause aseptic meningitis mostly at the time of sero conversion. It is difficult to assess the overall contribution of arbo viruses, but in epidemics a sizeable number of patients especially children will exhibit a benign illness with neurologic manifestations. This assumes special importance since Japanese encephalitis- an arboviral encephalitis is widely rampant in India. In the Central india , western equine encephalitis virus causes more cases of meningitis than the Eastern equine encephalitis virus,

which causes a more serious illness. The St Louis encephalitis virus may cause a meningitic picture in upto 60% of children affected. The lymphocytic choreomeningitis virus - an arena virus, is a rare cause of aseptic meningitis. The respiratory viruses - influenza A & B, adenoviruses and rhinoviruses can occasionally cause meningitis[19,20].

EPIDEMIOLOGY

The illness occurs at all ages and no racial differences are known. It tends to occur 3 times more commonly in males than females. Epidemiology of infectious meningitis reflects that of the infectious agent. Polio, Coxsackie and ECHO virus are spread by direct person to person transfer of infected oropharyngeal secretion or by feco-oral route. Enteroviruses are worldwide in distribution and humans are the only known natural hosts for these viruses. Infections with these viruses increase during late summer and early fall in the US[21]. The incubation period of enteroviruses varies widely[23].

Mumps meningitis has come down drastically in countries where the vaccine is widely used, but is still prevalent in India. Lymphocytic choreomeningitis occurs in individuals having close contact with rodents like mice, hamster etc. Herpes simplex is again worldwide in distribution, sporadic and non seasonal. Arboviruses tend to occur in fairly characteristic geographical settings. Tuberculous meningitis is still an important cause of childhood

hospital admissions in developing countries like India and has resurfaced in developed countries in association with HIV - AIDS.

PATHOPHYSIOLOGY

Infectious meningitis results when the protective barriers of the brain - skull, meninges and blood brain barrier are overcome by the infecting agent. Meningitis can result either by the hematogenous route (as in tuberculous meningitis, HIV meningitis, arboviruses, respiratory viruses etc.) or by neurotropic spread of the agent as in herpes virus, rabies and polio[24]. Predisposing factors include otitis media, immunosuppression, pneumonia, sinusitis and pre-existing diabetes.

CLINICAL FEATURES OF BACTERIAL MENINGITIS:

It can present as acute fulminantly over few hours or sub acute over days.

The classical clinical triad of meningitis is fever, headache and nuchal rigidity.

But the classic triad may not be present in some patients. Nausea, vomiting and photophobia may be the associated features. Altered level of conscious occurs in 77.5% of patients. Seizure may be seen in 20-40% of patients.

Focal seizures occur mainly due to focal arterial ischemia or infarction, cortical venous thrombosis with haemorhage or focal edema. Generalized seizure activity and status epilepticus might occur due to hyponatremia,

cerebral anoxia. Major cause of obtundation and coma in bacterial meningitis is due to raised ICP.

Meningococcal meningitis in some patients may have fulminant course, leading to death within hours of symptom onset. Meningococcemia may be associated with rash (diffuse erythematous maculopapular rash resembling viral exanthem, which turns rapidly into petechia). Petechia are present in trunk & lower extremities, in mucous membrane, conjunctiva and occasionally on palms & soles.

Nuchal rigidity (Neck stiffness) is pathognomic sign of meningeal irritation. False positive test for nuchal rigidity may be seen in older patients with cervical spine disease. Kernig's and Brudzinski's sign are also other signs of menigneal irritation. (But the sensitivity & specificity are not certain). There might be absent in very young or elderly patients or immune compromised patient or patients with severely depressed mental status.

Signs of increased ICP: Deteriorating or reduced level of consciousness papilledema, dilated poorly reacting pupils, sixth nerve palsies, decebrate posturing, cushing reflex (bradycardia, hypertention and irregular respirations)

Cerebral herniation is disastrous complication of raised ICP (Its incidence in Bacterial Meningitis is 1% to 8% of cases).

CLINICAL FEATURES OF VIRAL MENINGITIS:

This has common clinical manifestations with variations depending on the particular organism. Although in some cases, pointers to specific viral agents may exist, in most cases the clinical findings are not sufficiently distinct to allow a specific etiologic diagnosis. The most common symptoms are headache, fever, myalgias, malaise, chills, sore throat, abdominal pain, nausea, vomiting, photophobia, stiff neck and drowsiness. Occasionally the patient may exhibit altered consciousness in the form of confusion, drowsiness or visual hal1ucinations. Examination may reveal meningeal signs in the form of neck stiffness, Kernig's or Brudzinski's signs. Severe meningeal irritation may result in the patient assuming the tripod position with the knees and hips flexed, neck extended and arms brought back to support the thorax. Meningeal irritation is also manifested by jolt accentuation of headache. Worsening of headache on turning the head to and fro horizontally at 2-3 times per second constitutes a positive sign. Seizures, focal neurologic deficits or profound sensorial alteration are rare manifestations. Many viruses causing the illness also produce a characteristic rash. Papilledema or absence of venous pulsations upon fundoscopic examination suggests increased intracranial pressure24.In most cases, viral meningitis runs a mild course and is a self limiting, often transient illness. Some patients may exhibit a biphasic illness with nonspecific constitutional symptoms followed by meningitis. Presence of

severe or prolonged sensorial alteration should prompt the clinician to exclude other treatable conditions.

Enteroviruses

These are small non enveloped RNA viruses of the picorna virus family. They are subdivided into the ECHO viruses, Coxsackie and Polio viruses, each with several serotypes. More than 50 serotypes have been linked with meningitis. They are spread by hand to mouth contact and to a lesser extent by respiratory and fecal routes. Some enteroviral infections produce a rash that usually accompanies the onset of fever and persists for 4-10 days. Coxsackievirus A 5, 9 or 16 and Echoviruses 4,6,9,16 or 30 typically cause a maculopapular, nonpruritic rash confined to the face and trunk but sometimes involving extremities including palms and soles. Coxsackie A16 and rarely other group A serotypes may produce a vesicular rash on face, feet and oropharynx. Group A coxsackie virus[25] may also produce herpangina characterized by grey, vesicular lesions on the tonsillar fossae, soft palate and uvula. Enterovirus 71 has recently been recognized to cause hand-foot and mouth disease and neurological manifestations like aseptic meningitis, encephalitis and polio like paralysis in India. The genotype isolated here was distinct from that causing severe epidemics in the Asia-Pacific region[26].

Mumps Meningoencephalitis

Meningoencephalitis is the most frequent complication of mumps in childhood. Subclinical involvement, as evidenced by cerebrospinal fluid (CSF) pleocytosis has been reported in > 65% patients with mumps and clinical manifestations occur in >10% of patients. Males are affected 3-5 times as frequently as females and mortality is about 2%. Parotitis usually appears at the same time or following the onset of meningoencephalitis. Aqueductal stenosis and hydrocephalus have been associated with mumps meningoencephalitis.

HIV

HIV directly infects the central nervous system causing aseptic meningitis, encephalitis, leucoencephalopathy and myelopathy. Aseptic meningitis occurs mostly at the time of seroconversion. HIV encephalitis is characterised by progressive intellectual impairment, behavior disturbances, and sensorimotor deficits. As a result of immunodeficiency, patients are also more susceptible to toxoplasmosis, cryptococcosis, other fungal infections, cytomegalovirus and papova virus infection[27,28].

In contrast to viral meningoencephalitis, nonviral causes of aseptic meningitis usually have a more complicated course and must be considered because they can be managed with specific therapy.

Partially Treated Bacterial Meningitis

This may be confused with a non pyogenic or aseptic meningitis because CSF becomes sterile and cellular reaction changes from polymorphonuclear to lymphocytic. The condition is not benign or transient however rapid deterioration occurs in absence of antibiotic therapy. In India, this is an important differential diagnosis of tuberculous meningitis.

Tuberculous Meningitis

This remains an important cause of childhood hospital admissions, mortality and permanent disability in India. Tuberculosis produces a basal meningitis thereby causing damage especially to basal structures - brain stem, cranial nerves and basal ganglia. The illness usually has a subacute onset with 3 clinical stages. In stage 1, symptoms are nonspecific with irregular fever, irritability, occasional vomiting, headache, lethargy or malaise. Stage II is characterised by appearance of meningeal signs, convulsions or neurodeficits while stage III is accompanied by coma, decerebration and persisting deficits[29]. Prognosis is closely related to the stage of the disease in which it is diagnosed and treatment is started. A high index of suspicion is therefore extremely important to prevent permanent disability. A study from Lucknow revealed 5 clinico-laboratory features which are suggestive of TBM in a patients hospitalised with

meningoencephalitis: a prodromal stage of >7 days, extrapyramidal signs, focal deficits, optic atrophy and CSF pleocytosis with> 50% lymphocytes[30].

Lyme Disease

This is the most common vector borne disease in the US, caused by Borrelia burgdorferi - a fastidious, microaerophilic spirochete. Its prevalence in India is not known. In a study from Delhi, none of 27 patients presenting with mono/oligo arthritis of unknown etiology, 12 healthy blood bank donors, 25 patients with rheumatoid arthritis and 20 deer handlers were positive for IgG antibodies to Borrelia burgdorferi[31]. The illness is divided into early localised disease with a rash at the site of the tick bite often accompanied by fever, myalgia, headache and malaise; early disseminated disease with secondary erythema migrans lesions, constitutional symptoms, aseptic meningitis, cranial nerve palsies and carditis and late disease with chronic polyarthritis. Central nervous system manifestations are common in Lyme disease. Meningitis manifests several weeks after appearance of skin lesions, but while erythema migrans lesions are still present. Hypoglycorrhachia is not a prominent finding in the CSF. Facial nerve palsy, sometimes bilateral, may be observed. Diagnosis may be established by detection of specific IgM by ELISA, validated by Western Blot assay or by culturing the organism from a symptomatic patient. A study on differentiating features between Lyme meningitis and other aseptic meningitis showed that lyme meningitis

should be suspected in cases of meningitis with very low CSF neutrophilic counts and high protein levels associated with prolonged duration of symptoms, low grade fever and absence of pronounced signs of meningitis[32].

Brucellosis

This is a systemic infection caused by a small, aerobic, non spore bearing, nonmotile Gram negative coccobacillary bacteria, seen usually in persons living or working in close contact with animals, or consuming animal products such as raw milk or cheese made from raw milk. It is most common in the Mediteranean region, Asia, Africa, Mexico, South and Central America. Clinical features are extremely variable. In the acute form the illness presents with a flu like illness with fever, night sweats, malaise, anorexia, headache and myalgias. In the undulant form, symptoms are again fever, arthritis and epididymo- orchitis. Neurological involvement occurs in about 5% of patients. Diagnosis is confirmed by the isolation of brucella organisms from bacterial culture or increase over time of specific antibodies in blood. A study from Bikaner (Rajasthan) revealed 92 cases of brucellosis diagnosed on the basis of a history of contact with animals, fever, arthralgia and brucella antigen in serum in a titre of 1: 160or more. Of these, 12 had neurobrucellosis - 4 aseptic meningitis, 2 myelitis, 5 polyradiculo-neuropathy and 1 polyradiculomyeloencephalopathy[33].

Ehrlichiosis

Acute monocytic ehrlichiosis is a tick borne infection caused by a small, pleomorphic obligate intracellular bacteria that possess Gram negative cell walls. The mammalian host is the deer or other domestic ruminants. The usual presentation is with fever, headache, myalgia, anorexia and vomiting. Nearly two-third of children develop a maculopapular rash. The infection may occasionally produce aseptic meningitis. Other manifestations include photophobia, conjunctivitis, pharyngitis, lymphadenopathy, hepatosplenomegaly and arthritis. Laboratory tests may reveal pancytopenia and elevated hepatic transaminases, blood urea nitrogen and creatinine. Diagnosis is established by high single antibody titres or seroconversion. PCR amplification of DNA sequences may be helpful in early stage when antibodies may not be detected.

Leptospirosis

This is a zoonotic disease caused by the leptospiral spirochete. It may have an icteric or anicteric course. Anicteric leptospirosis usually presents as aseptic meningitis. A large epidemiological study in Kolenchery, Kerela after irrigation of dry lands picked up 976 cases of leptospirosis. The main reservoir for this zoonosis is the rat. In children and housewives, the main source of infection is a pet dog. IgM ELISA test is very sensitive though less specific for the diagnosis[34].

Syphilitic Meningitis

This is becoming more uncommon in the AIDS era. The secondary stage of the disease is heralded by a generalised nonprurutic rash, fever, headache, malaise and anorexia. Meningitis occurs in up to 30% of cases in this stage but may not produce neurological symptoms. Because of a lack of typical clinical presentation, CSF VDRL test should always be included in the diagnostic work up of aseptic meningitis.

Fungal Meningitis

Meningeal involvement can occur as the most serious manifestation of disseminated fungal infections. This occurs primarily in patients with AIDS, after organ transplantation, on immunosuppressive therapy or long term steroids. However, the most common fungal pathogen, Cryptococcus neoformans can occur in immunocompetent patients. Subacute or chronic meningitis is the most common clinical manifestation of disseminated cryptococcosis.Cryptococcal antigen assay in the CSF may be helpful in diagnosis.

Diagnosis

Brain imaging should be done prior to lumbar puncture (LP) in patients with decreased level of consciousness(somnolence, coma), focal neurological findings, papilloedema, recent head trauma, immuno compromised patients, known Malignant lesions or Central Nervous system Neoplasms.

MRI imaging of brain is superior to CT in view of its superior demonstration of areas of cerebral edema and ischemia. In patients with bacterial meningitis meningeal enhancement may be seen following gadolinium administration.

CSF findings in bacterial meningitis are

1. PMN leukocytosis (> 100 cells / µL) in 90%
2. Decreased glucose (< 40 mg / dl)
3. Increased protein (> 45 mg /dl in 90%)
4. Increased opening pressure (>180 mm H_2O in 90%)

CSF gram's stain organism is seen in > 60% of patients, CSF bacterial C/S may be positive in > 80% of patients, 16s rRNA conserved sequence broad - based bacterial PCR can detect even small numbers of viable and non viable organism in CSF. This PCR assay is useful in patients who have been previously exposed to antibacterial agents and in whom gram stain and cultures were non contributory.

LA (latex agglutination test) for the detection of bacterial antigens has a specificity of 95-100% for S.pneumoniae and N.meningitis, so a positive test is almost diagnostic of bacterial meningitis caused by these organisms. Limulus amebocyte lysate assay is rapid diagnostic test. It will detect gram - negative endotoxin in CSF. Useful for diagnosing gram negative bacterial meningitis.

Rapid, definitive differentiation of bacterial and viral infections of the central nervous system is a common clinical problem. Presence of severe obtundation, seizures and focal deficits suggest the former. Analysis of CSF for acid base changes, aminoacids, LDH and its isoenzymes, nitroblue tetrazolium test of CSF polymorphonuclear cells, immunoglobulins, C reactive protein and lactate have all been suggested as differentiating tests.

Laboratory Tests That May be Useful in Meningitis

Essential Tests

I In Blood

- Complete blood counts, ESR
- Acute and convalescent phase sera for virus specific IgG or IgM to enteroviruses, arboviruses, adenoviruses, LCMV, Ebstein Barr virus and HSV-2

II CSF Studies

- Cell count - total and differential
- Gram stain, Acid fast bacilli stain
- Bacterial culture and sensitivity
- C reactive protein
- Protein, glucose and gamma globulin
- Viral isolation
- PCR for viral agents and M tuberculosis

III Imaging

- Cranial CT scan

IV Other

- Viral isolation from throat and rectal swabs

As Indicated tests

I Blood Tests

- Antinuclear antibody, rheumatoid factor
- Sjogren's syndrome antigens A & B
- Serum protein electrophoresis
- Lyme antibody titre (ELISA)
- Serum amylase
- Viral isolation
- VDRL, Flourescent treponema I antibody absorption test

II CSF tests

- CSF lactate
- Cryptococcal antigen
- Latex agglutination test for H influenzae
- VDRL, FTA- ABS test
- Angiotensin converting enzyme (ACE) level

- Tuberculostearic acid
- Cytology
- Specific IgM antibodies to B burgdorferi, Brucella, Histoplasma and Coccidiodes species

III Imaging

- Xray chest
- MRI brain

IV Other

- PPD test

Laboratory Diagnosis

CSF : Suspicion of viral meningitis is based on the clinical presentation and presence of supportive CSF findings. CSF pressure is usually increased. CSF shows generally less than 500 cells/cu mm. Early examination may occasionally show acellular fluid or predominance of polymorphonuclear leukocytes. Typical mononuclear pleocytosis develops after 8-48 hours. CSF protein is elevated upto 100 mg % wheras glucose is normal or modestly decreased. Bacterial culture, Gram stain and bacterial antigen tests are uniformly negative. Levels of tumour necrosis factor (TNF) and lactate are low. Viral isolation from CSF is the standard criterion for diagnosis but is not positive in all patients.

Measurement of interferon alpha levels in CSF provides evidence of active viral invasion of the CNS but this test is not widely available. IgG index which is derived by calculating the ratios of IgG and albumin in CSF and serum is another indicator of intrathecal synthesis of antibodies. Specific IgG ratios in CSF and serum can also be used to identify infection with specific viruses but these are seldom helpful in the early stages of the illness[35].

The polymerase chain reaction (PCR) is an important advance in diagnosis of infectious meningitis[36,37]. In recent years, it has become available for more and more agents. Stellrecht et al (2002)[38] studied the impact of enteroviral Reverse Transcriptase PCR assay (RT-PCR) in the diagnosis and management of enteroviral meningitis in 1056 hospitalised patients. They concluded that RT-PCR for enteroviral meningitis is an important tool in the diagnosis with meningitis and nonspecific febrile illness which translated into shortened hospital stay and significant health care savings.

Viral isolation

Besides CSF, arboviruses and enteroviruses can be isolated from blood but are seldom recoverable once clinical meningitis has set in. Specimen for viral culture from respiratory secretions, throat swab, CSF, blood, urine and stool should be taken as early in the illness as possible. Coxsackie and Echo viruses can be isolated from stool or throat swabs. Mumps virus can be

isolated from saliva or throat swabs, HSV-2 from genital lesions and LCMV from blood.

Serology

Seroconversion as demonstrated by a 4 fold rise in antibody titre in acute and convalescent phase sera can be helpful in making a diagnosis. However, virus specific IgM provides a quick, early and accurate diagnosis. As IgM does not cross the blood brain barrier, presence of CSF IgM is highly suggestive of brain invasion by the pathogen.

Imaging

CT or MRI brain is not helpful in the usual viral meningitis. These imaging techniques may help to exclude other diagnoses. Imaging is particularly helpful in later stages of tuberculous meningitis which shows basal enhancement and hydrocephalus[39].

Nigrovic, Kuppermann & Malley (2002) developed a multi variable prediction model to distinguish bacterial from aseptic meningitis in a retrospective cohort of 696 children aged 29 days to 19years. 125(18%)had bacterial meningitis and 571 (82%) had aseptic meningitis. Significant predictors for bacterial meningitis were gram stain of CSF showing bacteria, CSF protein ≥ 80 mg/ dl, peripheral absolute neutrophil count ≥10,000, seizure before or at presentation and CSF absolute neutrophil count ≥1000. A score giving 1 point for each of these predictors except the first which

was given 2 points accurately identified patients with bacterial and aseptic menigitis with sensitivity of 87%[40].

TREATMENT

If Bacterial Meningitis is our suspicion or in some patients with decreased level of consciousness (somnolence, coma), focal neurological findings, papilloedema, recent head trauma, immuno compromised patients, known Malignant lesions or Central Nervous system Neoplasms, empirical therapy may be started before obtaining a neuro imaging or proceeding for lumbar puncture.

Blood cultures should be sent immediately, empirical antibacterial therapy and adjuvant dexamethasone therapy should be started. LP can be done prior to neuro imaging in patients with normal level of consciousness and no papilloedema or no focal neurological deficits or no history of recent head trauma.

Petechial skin lesions if present should be biopsied (Biopsy - Gram stain may reveal organism). Emperical therapy of suspected community acquired bacterial meningitis include combination of dexamethasone, third or fourth generation cephalosporin (ceftriaxone, cefotaxime or cefepime) and vancomycin plus acyclovir (as HSV encephalitis is one of the important differential diagnosis).

Ceftriaxone and cefotaxime had good coverage for susceptible S.pneumonia, N.Meningitis, group B streptococci and H.Influenza. Cefepime has been demonstrated to show activity against P. aeuruginosa and enterobacter species.

Ampicillin should be added empirically, for coverage of L.monocytogenes in those □55years of age, impaired cell mediated immunity, pregnancy, malignancy, organ transplantation, patient on immuno suppressive therapy.

Metronidazole can be added to empirical regimen to cover gram negative anaerobes in patients with otitis, sinusitis or mastoiditis.

In hospital acquired meningitis, meningitis following procedures, Staphylococci and gram negative organism including P.aeuruginosa should be covered, so emperical therapy should include vancomycin and meropenem/ceftazidine / cefepime.

Specific antitherobial therapy:

Pneumococcal meningitis:

Patient should be treated with cephalosporin (ceftriaxone, cefotaxime or cefepime) and vancomycin. Ceftriaxone, cefotaxime MIC $\leq$ 0.5 µg/ ml, treatment with the above is usually adequate. If MIC > 1 µg/ml vancomycin is drug of choice. Rifampin can be added to vancomycin for its synergistic effect. 2 week course of intravenous anti microbial therapy is necessary.

Repeat LP should be done 24-36 hr to look for sterilization of CSF. Failure to sterilize the CSF, should raise the suspicion of antibiotic resistance. Intraventicular vancomycin may benefit in patients who do not respond with intra venous vancomycin.

Meningococcal meningitis:

Penicillin is the antibiotic of choice, if penicillin and ampicillin resistance was found, ceftriaxone or cefotaxime should be substituted. 7 day course is adequate for uncomplicated cases. Index case and all close contacts should receive chemoprophylaxis with 2 day regimen of rifampin(600 mg q12h for 2 days in adults). Rifampin is not recommended in pregnant women. Alternatively , one dose of azithromycin (500mg) or one intra muscular dose of ceftriaxone (250mg) can be given.

Listeria:

Ampicillin for at least 3 weeks, Gentamicin (2mg/ kg loading dose, then 7.5 mg / kg per day every 8 h) can be added in critically ill patients. Trimethoprim (10-20 mg / kg per day) and Sulfamethoxazole (50-100 mg/kg per day) given every q6h is an alternative for penicillin allergic patients.

Staphylococcal meningitis:

Susceptible strains of S.aureus or CONS are treated with nafcillin. Vancomycin is drug of choice for patients with Methicillin resistant

staphylococci & patients allergic to pencillin. If CSF not sterilized after 48 hours of intravenous vancomycin therapy, then intra ventricular or intrathecal vancomycin 20 mg once daily can be added.

Gram negative bacillary meningitis:

Third generation cephalosporin (ceftriaxone, cefotaxime or ceftazidime) are useful. In order to cover P.aeuruginosa meropenem, ceftazidime or cefepime is better choice. 3 week course IV antibiotic therapy as recommended.

Adjunctive therapy:

Bacterial antibiotics release bacterial cell wall components which leads to production of inflammatory cytokine IL - 1 β and TNF α in the subarachanoid space. Dexamethasone should be given 20 min before antibiotic therapy (Rationale behind this is that dexamethasone inhibits synthesis of TNFα by macrophages and microglia only if it is administered before these cells are activated by endotoxin). Dexamethasone by acting by the above mechanism decreases CSF outflow resistance and stabilizes the blood brain barrier. Its efficiency for decreasing meningeal inflammation and neurological sequelae such as incidence of sensorineural hearing loss was also demonstrated.

A prospective European trial of adjunctive therapy for acute bacterial meningitis done in 301 adults found that the number of unfavorable out comes

(15 vs 25% p=0.03) including death (7 vs 15%, p=0.04) .These results are more strong in patient with pneumococcal meningitis.

Dexamethasone (10mg intravenously) and same dose can be repeated every 6 hours for 4 days.

Viral Meningitis

Many patients can be treated after an initial lumbar puncture. Those who have seizures, altered consciousness or severe symptoms or those in whom the diagnosis is in doubt should be hospitalised. Treatment is mostly supportive and includes analgesics, antipyretics, anti emetics, maintainence of fluid balance and prevention and treatment of complications. Antiviral therapy is available against HSV, varicella and cytomegalovirus. Acyclovir, valacyclovir and foscarnet are used for herpes or varicella infections and ganciclovir is used for cytomegaloviral infection.

Specific antimicrobial therapy would be required for infectious agents for tuberculous meningitis, antitubercular therapy with 4 drugs - Streptomycin, isoniazid, rifampicin and pyrazinamide for the initial 2 months followed by 3 drugs for another 10 months is generally recommended, along with 4-6 weeks of steroids initially. Antifungal agents that can be used are amphoterecin B, fluconazole and flucytosine.

COMPLICATIONS

Seizures, even status epilepticus can sometimes occur with aseptic meningitis but prophylactic anticonvulsants are not recommended. If seizures occur, they should be controlled with phenytoin and phenobarbital.

A variable component of encephalitis may be seen with viral meningitis. Mumps meningoencephalitis can result in sensorineural deafness and aqueductal stenosis causing hydrocephalus. Complications of tuberculous meningitis include hydrocephalus, infarcts, neurological deficits, cranial nerve palsies, epilepsy and mental regression.

PROGNOSIS

Viral meningitis is usually a benign disease, with low rates of morbidity and mortality. Full recovery occurs within 5-14 days in most patients. Fatigue, light headedness and asthenia may persist for a few months in some patients. Other nonviral infectious meningitis is not so benign, however, Tuberculous meningitis is a particularly dangerous illness with high rate of mortality and permanent sequelae unless diagnosed and treated very early.

PREVENTION

Patients with measles, chickenpox, rubella or mumps must be isolated. Strict hand washing especially after nappy changes are important in preventing spread of enterovirus infections. Effective vaccines are available for polio, measles, mumps, varicella and rubella. Arboviral vaccines are also available and should be used for populations living in or visiting endemic areas.

RESULTS

In this study, we collected 50 consecutive patients, who presented with acute meningo-encephalitis and fulfilled the inclusion and exclusion criteria of study protocol.

SEX RATIO:

Among the 50 patients, 33 patients were (66%) males and 17 patients were females.

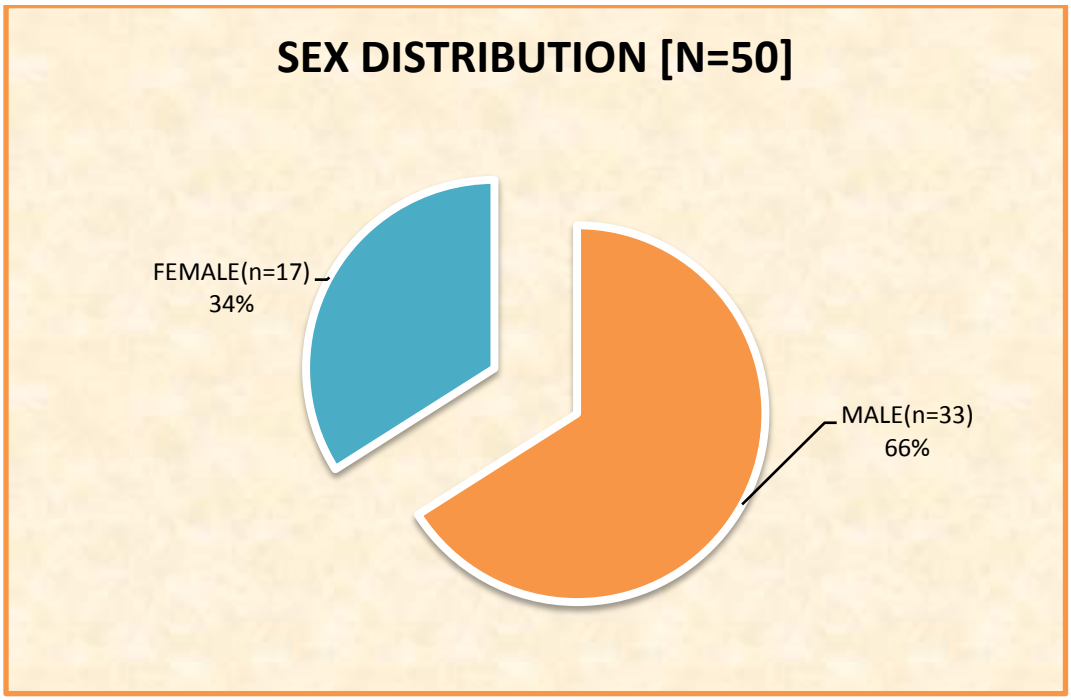


FIGURE-1

AGE :

TABLE-1

AGE	MALE	FEMALE	TOTAL	(%)
18 -30	12	5	17	34%
31 – 50	17	5	22	44%
51 – 60	2	7	9	18%
>60	2	0	2	4%
TOTAL	33	17	50	100%

39 patients in our study were young adults (<50 years of age group). 9 patients were in the 50-60 years age group; Only 2 patients were elderly adults (one 64 years, and another 86 years).

CLINICAL PRESENTATION

Among the 50 patient with meningo-encephalitis in this study, the common initial presenting symptoms were fever, headache and altered sensorium. Fever was the most common initial presenting symptom. 41 patients (82%) had fever and 37 patients had headache.

Headache was associated with vomiting in some of the patients. 32 patients had both fever and headache. 31 patients had altered sensorium in the course of illness, varying from drowsiness to deep coma.

Only 18 patients had all the three triad – headache, fever and altered sensorium.

TABLE-2

PREVALENCE OF POSITIVE CLINICAL PRESENTATION		
CLINICAL PRESENTATION	**N**	**(%)**
Headache	37	74%
Fever	41	82%
Seizures	6	12%
Vomiting	24	48%
Altered mental status	31	62%
CSF Rhinorrhea	4	8%
Hemiparesis	4	8%
Speech Disturbances	2	4%
Cranial Nerve Palsy	4	8%

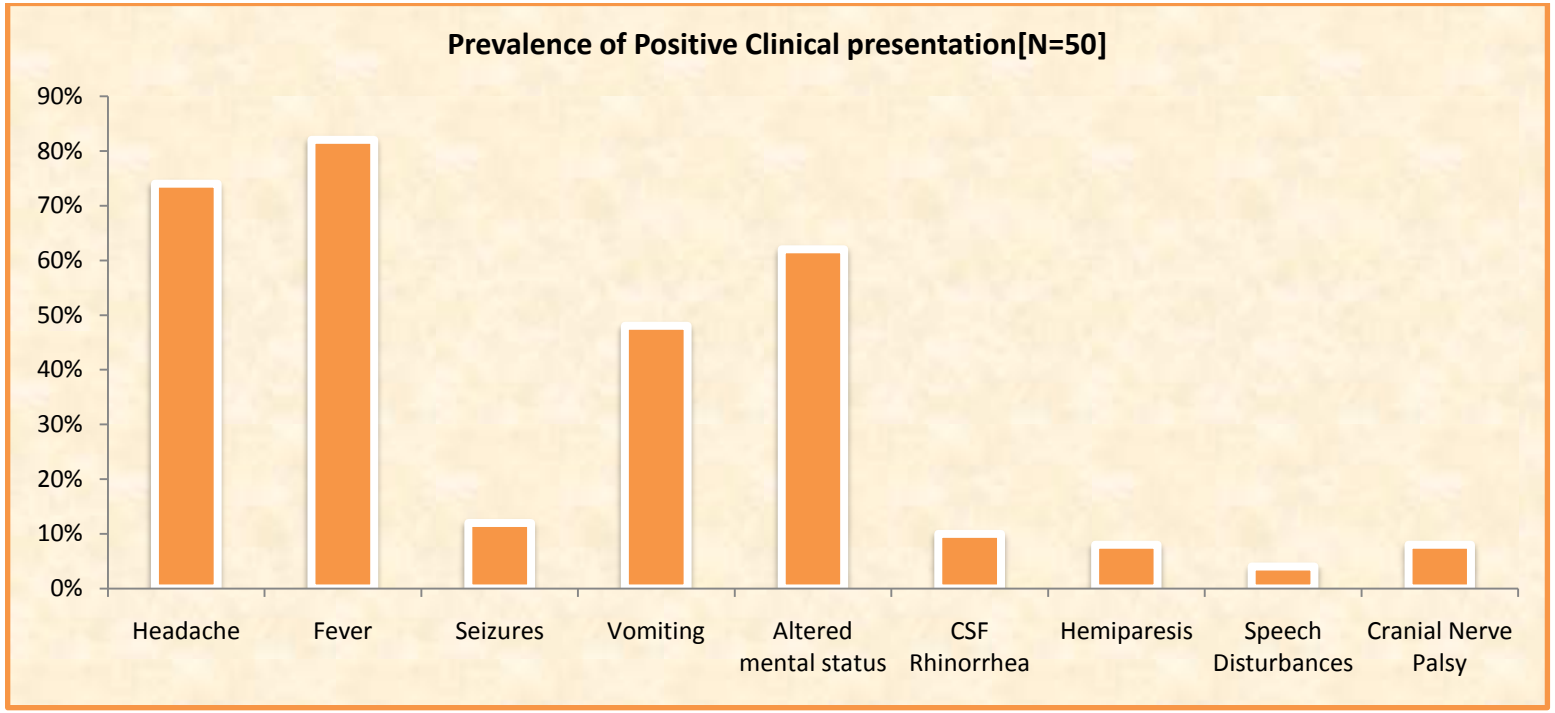


FIGURE: 2

2 patients had atypical presentation. A 60 year old female with HIV infection presented with hemiparesis without fever, headache or altered sensorium. Neuroimaging suggested the diagnosis of cerebral toxoplasmosis. One patient without HIV infection presented with altered sensorium without fever or headache. His CSF analysis confirmed the diagnosis of cyrptococcal meningitis.

SEIZURES

6 patients had seizures during the course of illness. 5 patients had generalized tonic clonic seizures. One patient had focal motor seizures.

TABLE:3

SEIZURE		
SEIZURE	**F**	**(%)**
GCTS	5	10%
FOCAL	1	2%
NO	44	88%

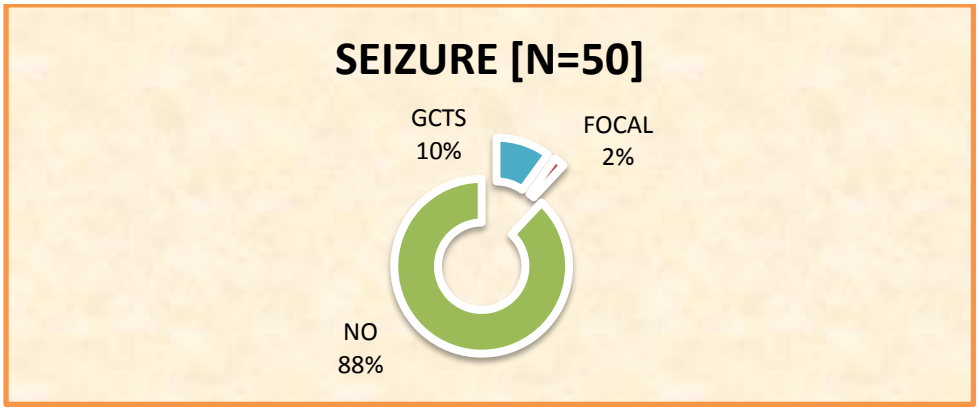


FIGURE:3

Among the 6 patients only one patient had parenchymal lesion in the MRI (granuloma). Other 3 patients had only meningeal enhancement and 2 patients had normal MRI.

CLINICAL FINDING

Only 22 patients had neck stiffness. Remaining 28 patients did not have neck stiffness, even though there is meningeal involvement. Fundus examination showed papilledema in only 5 patients.

TABLE: 4

PREVALENCE OF POSITIVE CLINICAL FINDINGS		
CLINICAL FINDINGS	F	(%)
Neck Stiffness	22	44%
Papilloedema	5	10%

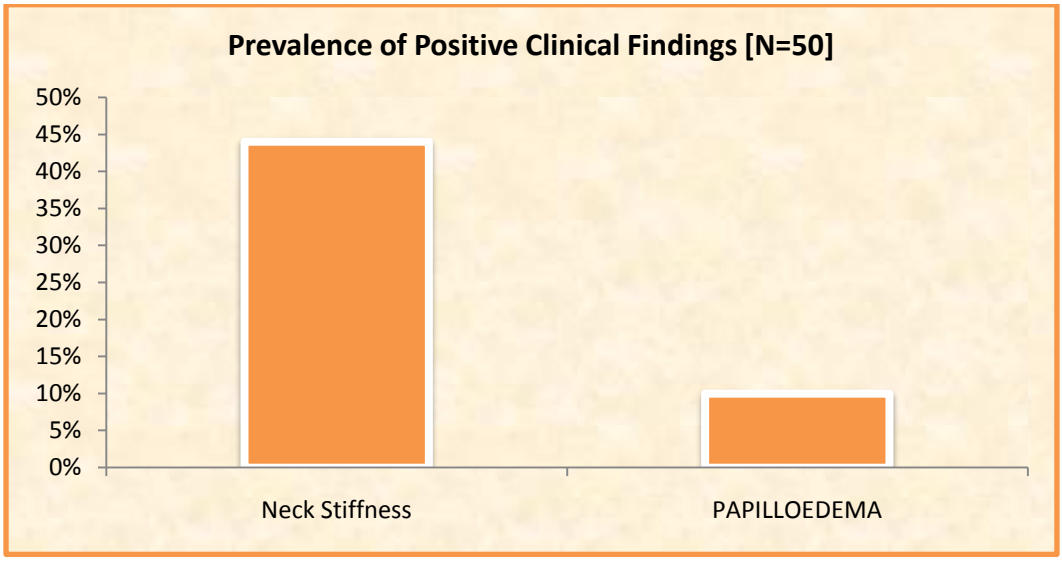


FIGURE:4

Only 7 patients had neurological deficits. 3 patients had hemiparesis, one patient had hemiparesis and aphasia. 4 patients had cranial nerve paralysis (Lateral Rectus palsy and facial weakness).

Among patient with altered sensorium, 10 patients had significant deterioration in consciousness with Glascow coma scale less than 10; One patient with Pyogenic Meningitis (case no :4) had deep coma with GCS 3/15 throughout the hospitalization with poorly reacting pupils. He had extensive vasculitic infarcts in the bilateral cerebral hemisphere and brainstem ; Among the remaining 9 patients only 2 patients had normal MRI. 7 patients had abnormal MRI with meningeal enhancement , granuloma or hydrocephalus; All these 10 patients were on ventilatory support in ICU, until the consciousness improved.

TABLE: 5

PREVALENCE OF MRI FINDINGS		
MRI FINDINGS	F	(%)
Meningeal Enhancement	25	50%
Hydrocephalus	6	12%
Granuloma	5	10%
Vasculitic infarcts	5	10%

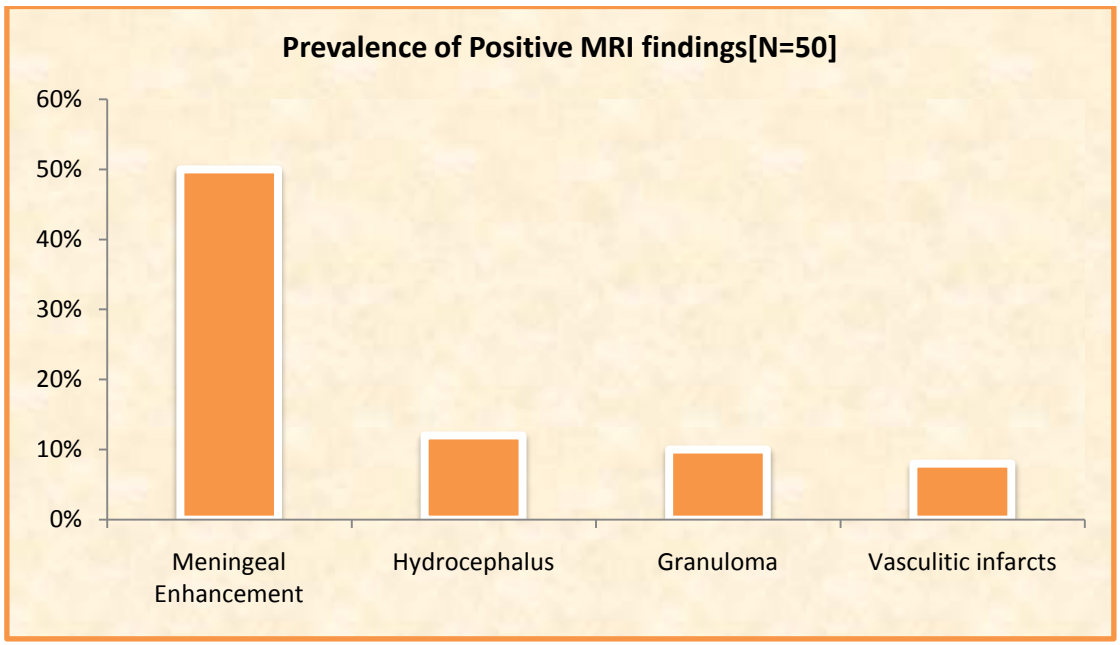

Prevalence of Positive MRI findings[N=50]
60%
50%
40%
30%
20%
10%
0%
Meningeal Enhancement
Hydrocephalus
Granuloma
Vasculitic infarcts

FIGURE: 5

RISK FACTOR:

4 patients had CSF rhinnorhea as the cause of their meningitis. 3 patients had CSF rhinorrhea due to past head injury. One patient had non traumatic CSF rhinorrhea.

TABLE:6

PREVALENCE OF CSF RHINNORHEA		
CLINICAL VARIABLES	F	(%)
CSF RHINORRHEA	4	8%

6 patients had HIV infection with low CD4 counts which was the cause of the opportunistic CNS infections with meningoencephalitis.

TABLE:7

PREVALENCE OF PARAMETER		
Parameter	F	(%)
HIV infection	6	12%

ETIOLOGY OF MENINGO ENCEPHALITIS

In our study, etiology of meningo encephalitis and the probable organisms responsible for meningoencephalitis was diagnosed on the basis of CSF analysis and MRI brain findings. Gram stain and CSF culture and sensitivity helped to isolate the bacteria in case of pyogenic meningitis; Patient's who presented with subacute meningitis, CSF lymphocytic pleocytosis, elevated CSF protein and absent cryptococcal antigen in CSF were diagnosed as probable tuberculous meningitis ;MRI evidence of basal meningeal exudates, hydrocephalus, tuberculous granuloma in the brain helped to reach the diagnosis of tuberculous meningitis.

CSF PCR technique helped to reach diagnosis in patients with Herpes simplex encephalitis, Aspergillus Meningitis and some cases of tuberculous meningitis.

Among 50 patients, 29 patien ts were diagnosed as Tuberculous meningitis. 8 patients were diagnosed as pyogenic meningitis; 8 patients were diagnosed as viral meningo encephalitis. Among the 8 patients with viral meningoencephalitis, 2 patients had positive HSV PCR in the CSF. No organism could be found in the remaining 6 patients. 2 patients had cryptococcal meningitis (One patient with HIV infection, another patient without HIV infection). 2 patients had cerebral toxoplasmosis and one patient had aspergillus meningitis.

TABLE:8

ETIOLOGY		
ETIOLOGY	**N**	**(%)**
Tuberculous Meningitis	29	58%
Acute Pyogenic Meningits	8	16%
Viral MeningoEncephalitis	8	16%
Cryptococcal Meningitis	2	4%
Cerebral Toxoplasmosis	2	4%
Aspergillus Meningits	1	2%
Total	50	100%

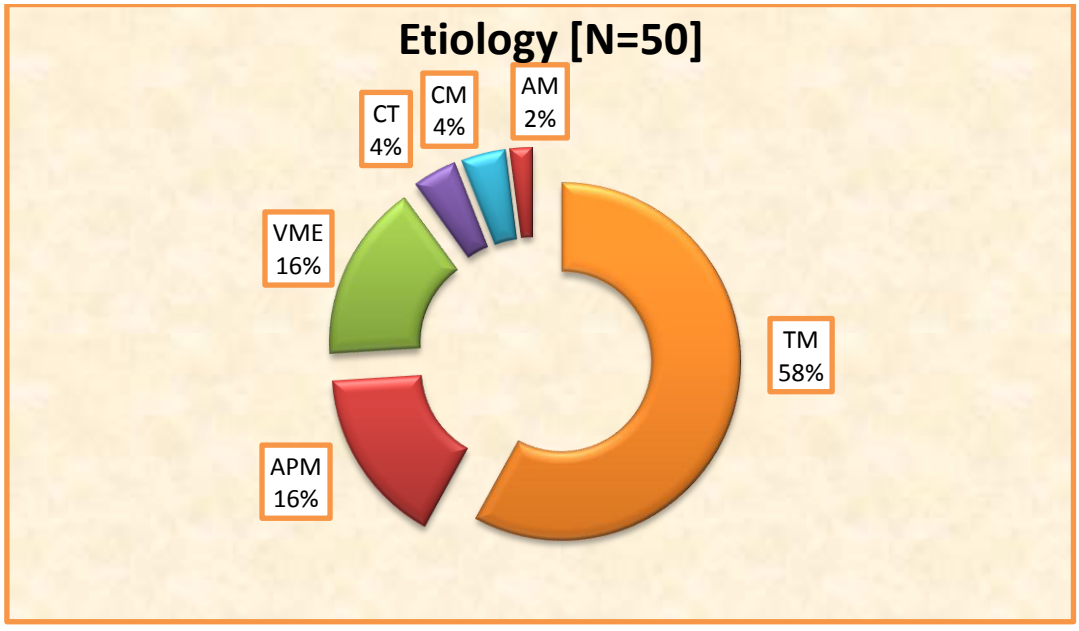


FIGURE:6

TABLE: 9

MODE OF ONSET		
MODE OF ONSET	**N**	**(%)**
ACUTE [< 1 WEEK]	23	46%
SUB ACUTE[1-4 WKS]	23	46%
CHRONIC [>4 WKS]	4	8%
Total	50	100%

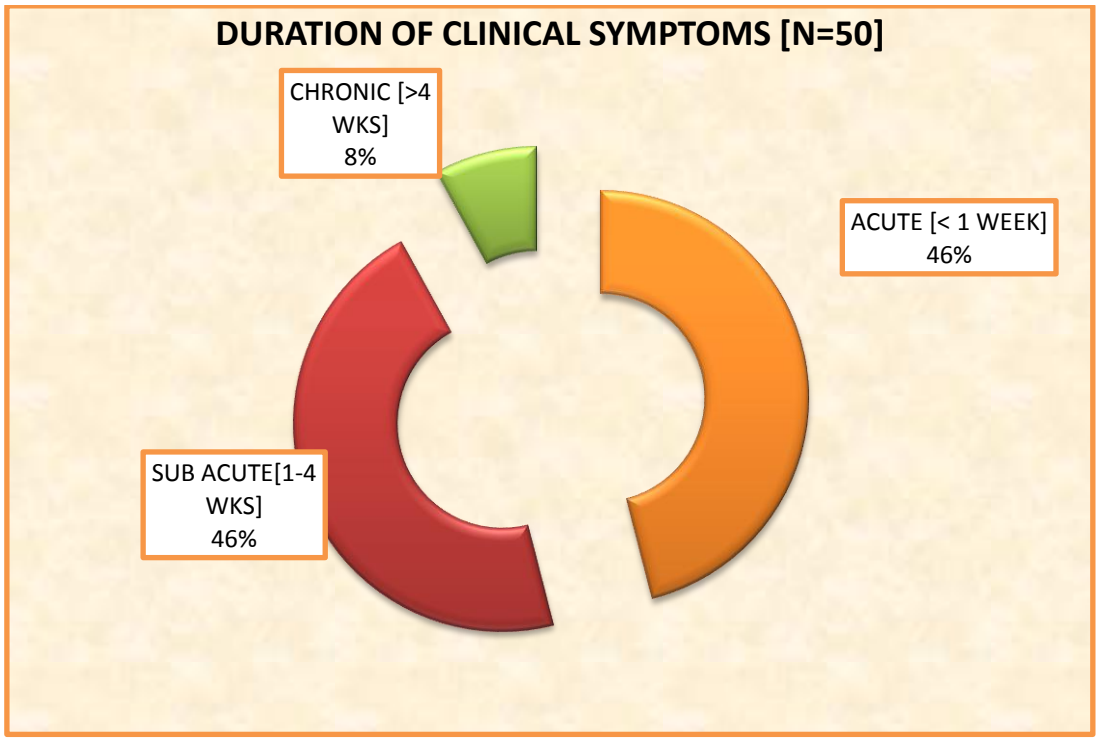


FIGURE:7

TABLE:10

COURSE OF ILLNESS ACUTE [< 1week] [n=23]		
ETIOLOGY	N	(%)
Tuberculous Meningitis	4	17%
Acute Pyogenic Meningits	8	35%
Viral Meningoencephalitis	8	35%
Cryptococcal Meningitis	1	4%
Cerebral Toxoplasmosis	2	9%

TABLE 11

SUB ACUTE [1 - 4 week] [n=23]		
CLINICAL VARIABLES	F	(%)
Tuberculous Meningitis	21	91%
Cryptococcal Meningitis	1	4%
Asperillus Meningits	1	4%

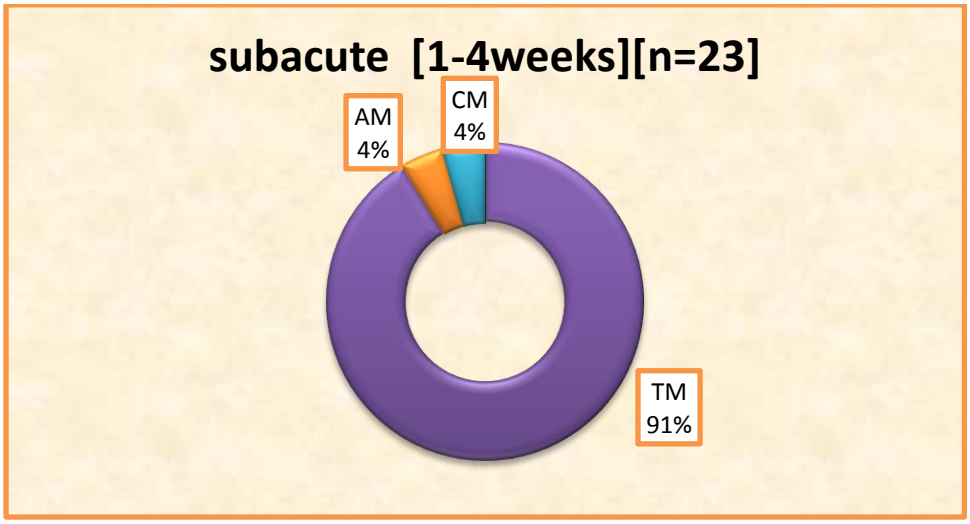


FIGURE:8

TABLE:12

CHRONIC [> 4 weeks] [n=4]		
ETIOLOGY	F	(%)
Tuberculous Meningitis	4	100%

TABLE:13

ASSOCIATION OF MODE OF ONSET WITH DIAGNOSIS				
ETIOLOGY	**ACUTE**	**SUB ACUTE**	**CHRONIC**	**Total**
Tuberculous Meningitis	4	21	4	29
Acute Pyogenic Meningits	8	0	0	8
Viral Meningoencephalitis	8	0	0	8
Cryptococcal Meningitis	1	1	0	2
Cerebral Toxoplasmosis	2	0	0	2
Aspergillus Meningits	0	1	0	1
Total	23	23	4	50

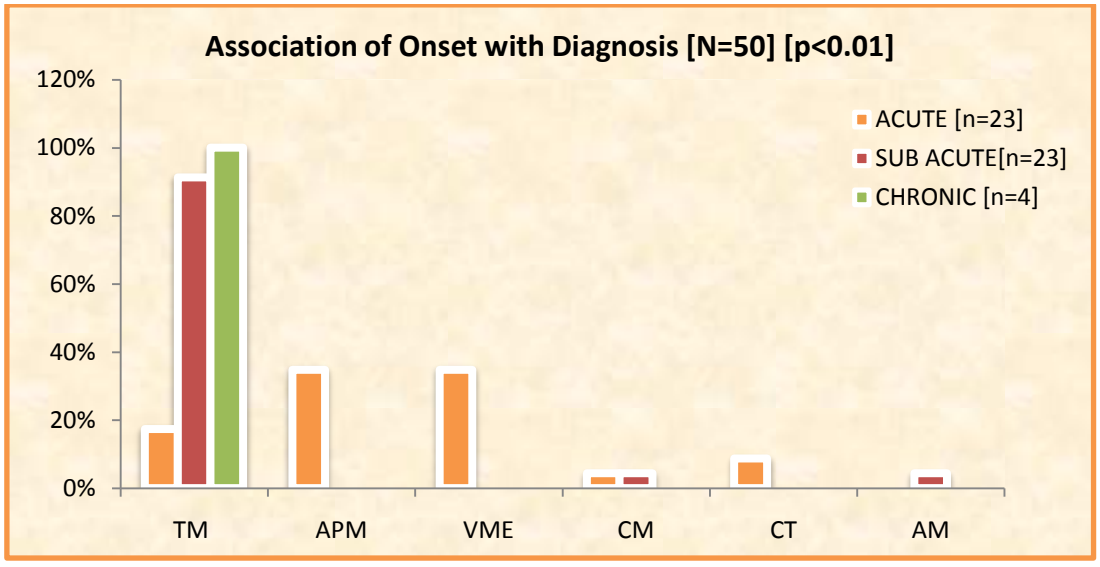


FIGURE: 9

Outcome: outcome at the end of one month by Barthel index Scoring was done . Among 50 patients, 47 patients recovered completely without neurological deficits.

1 case had Barthel index zero. Another 2 patients had rapidly progressive fulminant course and were succumb to the illness by the end of 1 month.

TABLE: 14

ASSOCIATION OF OUT COME WITH DIAGNOSIS							
Diagnosis							
OUTCOME	TM	APM	VME	CM	CT	AM	Total
YES[n=47]	29	6	8	1	2	1	47
NO[n=3]	0	2	0	1	0	0	3
TOTAL	29	8	8	2	2	1	50

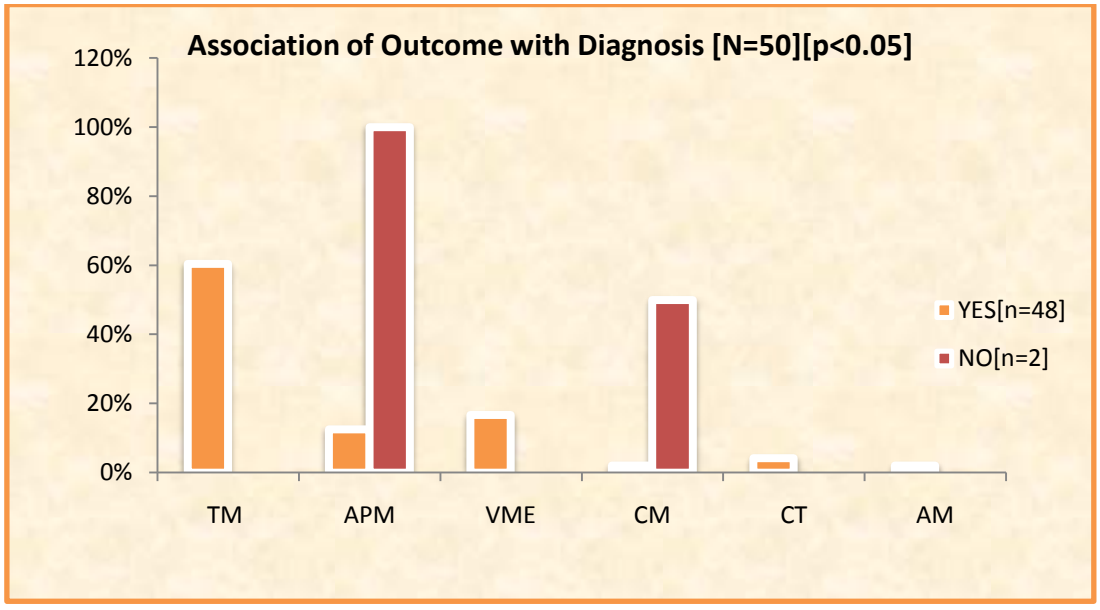


FIGURE: 10

DISCUSSION

Meningitis and encephalitis constitute more than 95% of all CNS infections. Remaining small percentage of CNS infections involve the spinal cord and spinal meninges alone and result in myelits, myeloradiculitis or spinal meningitis . In our study, we tried to analyze the major portion of CNS infections i.e. Meningitis and encephalitis. The name ‘meningitis’ is coined when inflammation occurs predominantly in the meningeal coverings and always adjacent brain parenchyma is also inflammed in meningitis. The term ‘encephalitis’ is coined when inflammation involves the brain parenchyma predominantly and adjacent meninges also often involved in encephalitis.

Clinical presentation are almost similar in meningitis and encephalitis that include fever, headache, seizures and altered sensorium. Signs of meningeal irritation, like neck stiffness and positive kernig sign occurs in most of the patients with meningitis and is often absent in patients with predominant encephalitis. Sometimes, neck stiffness may be absent in patients with predominant meningitis especially in subacute meningitis and meningitis in infants and elderly adults. So, the term meningitis and encephalitis are not exclusive.

Due to the overlapping clinical features, the term ‘meningoencephalitis’ can be used to describe the intracranial CNS infections. In this study we analyzed 50 consecutive patients of meningo encephalitis admitted in PSGIMSR

between June 2014 and June 2015. Although epidemiological studies are not available to analyze the accurate incidence of meningo encephalitis, several epidemiological data are available separately for bacterial, viral and fungal infections of the central nervous system. This study is unique that we analyzed all the cases of meningo encephalitis and we are able to produce small epidemiological data about the incidence of common organisms responsible for meningo encephalitis in a tertiary care center level.

CLINICAL PRESENTATION IN THIS STUDY

According to the mode of onset, we had divided all the patients into three groups.

I. Acute meningo encephalitis: patients who presented with sudden onset and rapidly progressive clinical course were grouped as acute meningo encephalitis. Patient who were admitted in hospital within one week of symptom onset were classified under this group.
II. Subacute meningo encephalitis: Patients who presented less dramatically and gradual progression of clinical course over weeks were grouped as subacute meningoencephalitis. Patients who were admitted in the hospital in-between one week to 4 weeks of onset of illness were classified under this group.
III. Chronic meningo encephalitis: Patient who had symptoms of more than 4 weeks duration were classified under this group.

The common presenting symptoms were fever (82 %), Headache(74 %) and altered sensorium (62 %). Among 50 patients with meningoencephalitis, 9 patients did not have fever during the course of illness. In these 9 patients , 2 patients had cryptococcal meningitis, 1 patient had cerebral toxoplasmosis, 1 patient has aspergillus meningitis and remaining 5 patients had tuberculous meningitis ; 28 patients did not have neck stiffness at all. This indicates that absence of fever or neck stiffness does not exclude the possibility of infectious meningoencephalitis.

Acute meningo encephalitis

23 patients (46%) in the study presented with acute meningo encephalitis. Among 23 patients, 8 patients had acute pyogenic bacterial meningitis, 8 patients had acute viral meningoencephalitis. 4 patients had acute presentation of tuberculous meningitis. 1 patient was diagnosed as Cryptococcal meningitis and remaining two had cerebral toxoplasmosis.

Acute Pyogenic Meningitis

There was no difficulty in diagnosing patients with acute pyogenic meningitis. All 8 patients presented hyperacutely with sudden onset of fever, headache and rapidly deteriorating conscious level within 1-2 days of symptoms onset. All 8 patients were young adults in 20-40 years age group. All patients had altered sensoium with reduction in conscious level. Patients were diagnosed as pyogenic meningitis on the basis of typical CSF

findings. All patients had high protein, low sugar and very high neutrophil count in the CSF (> 1000 cells/mm3 in most of the patients).

The probability of visualizing bacteria on a gramstain depends on the specific bacterial pathogen, CSF concentration of bacteria and technique.

Bacteria	**Probability of getting positive gramstain**
Streptococcus Pneumoniae	90%
H. influenzae	86%
Neisseria meningitides	75%
Gram negative bacilli	50%

The yield of gram stain may be <20% if the patient received antibiotic priorly.

Among 8 patients, in 5 patients confirmatory microbiological diagnosis was reached. In 2 patients, CSF culture showed growth of pneumococci, in 1 patient blood culture grew staphylococcus aureus and in another patient blood culture had pneumococcus growth, and in one patient gramstain showed gram positive cocci in pairs strongly suggestive of pneumococci, but culture was negative; In remaining 3 patients culture did not grow organisms; all these 3 patients received antibiotics in the initial hospital (before LP) from where they were referred. But, very high neutrophil count in the CSF suggested the diagnosis of acute pyogenic meningitis.

In a restrospective study of 305 patients with acute bacterial meningitis, treated in a hospital in UK, 53 patients (17.4%) received antibiotic prior to admission. Among 53 patients, death occurred only in one patient (1.9%) compared to 12% death (30 patients) in 252 patients who had not received antibiotic prior to admission. This study indicates the importance of early institution of antibiotic therapy. 41,42

All our 8 patients received empirical antibiotic therapy with Inj. ceftriaxone 2gm IV BD and Inj. Vancomycin 1gm IV bd which was continued throughout the course of illness irrespective of sensitivity reports (Due to high incidence of penicillin resistance for pneumococci in the recent reports).

Surprisingly, 4 patients (50%) had history of CSF rhinorrhea before the onset of illness. Of these, 3 patients had severe head injury in the past which was the cause of CSF rhinorrhea. Remaining one patient with HIV infection had CSF rhinorrhea and presented with meningitis. Initially clinically possibility of tuberculous or cryptococcal meningitis was considered due to co-existent HIV infection with low CD4 count. But her CSF analysis confirmed the diagnosis of pneumococcal meningitis. Her MRI brain revealed defect in the anterior cranial fossa (Probably congenital) which was the cause of CSF leak. One patient (Case 43) had recurrent episodes of pyogenic meningitis due to persistent CSF leak through nose. Last one was the third episode. After recovering from meningitis, he was referred to Neurosurgery Department for the correction of bony defects. In

all patients with acute pyogenic meningitis, history should be carefully elicited for CSF rhinorrhea, preferably directly from the patient once the patient regained full consciousness.

Among 8 patients, 6 patients recovered completely without residual deficits, but 2 patients had fulminant meningitis with severe neurological disability. One 40 years old male patient (case no 4) had fulminant pneumococcal meningitis. He had extensive cerebral edema and multiple infarcts in bilateral brain parenchyma with severe brainstem dysfunction. Though treatment was initiated appropriately, severe brain stem dysfunction could not be recovered. He was deeply comatosed with GCS 3/15 throughout the hospital course and subsequently expired. Another patient (case no 22), 27/M also had fulminant pneumoccal meningitis with extensive vasculitic infarcts in bilateral cerebral hemisphere and brainstem ; He had bilateral conjugate gaze paralysis of eye balls and quadriparesis due to large pontine infarct, but gradually his consciousness improved. He was weaned from ventilator, tracheostomy was done. At the end of one month he was able to sit with the help of 2 persons, had power 2-3 in all 4 limbs and was on Ryles tube feeding.

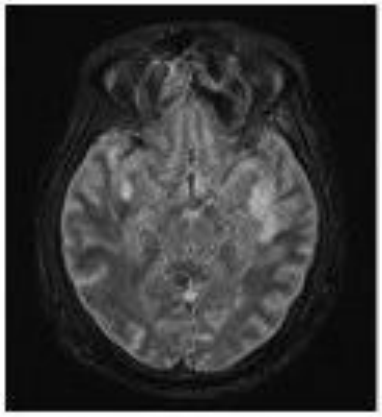
Despite early diagnosis and appropriate treatment some patient with acute pyogenic meningitis may have fulminant course with severe neurological disability.

CASE 43: ACUTE PNEUMOCOCCAL MENINGITIS

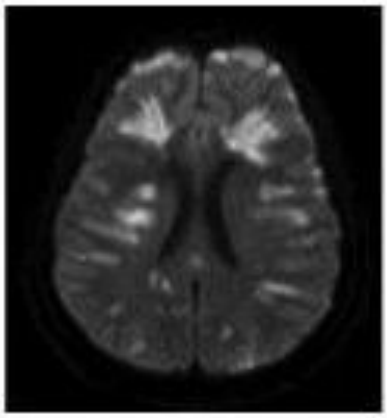
PURULENT CSF ON DAY 1

CLEAR CSF AFTER TREATMENT

CASE NO 4: ACUTE PYOGENIC MENINGITIS

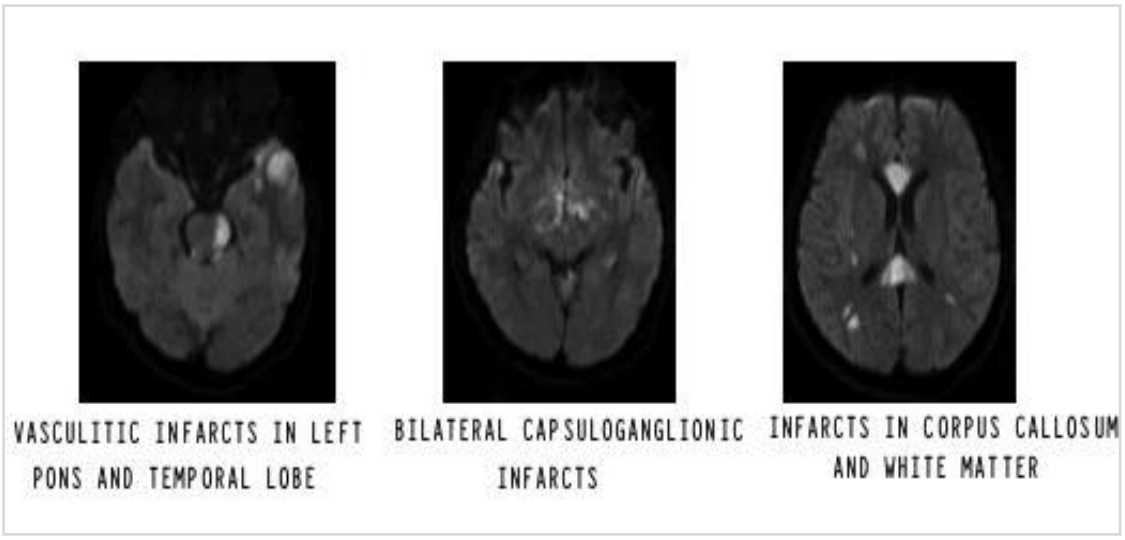


MRI FLAIR SHOWS EXTENSIVE BRAIN EDEMA



MRI DWI- EXTENSIVE VASCULITIC INFARCTS IN B/L WHITE MATTER

CASE NO 22: ACUTE PYOGENIC MENINGITIS



Acute Viral Meningo Encephalitis

In our study 8 patients were diagnosed to have acute viral meningoencephalitis. In a patient admitted with acute meningo encephalitis, establishing the diagnosis of viral etiology is more difficult than diagnosing bacterial meningitis. Because, isolation of virus by viral culture is very difficult in contrast to the high sensitivity of gramstain technique and bacterial culture. Comprehensive viral PCR technique is necessary to identify the common viruses in CSF. We diagnosed viral meningo encephalitis on the basis of CSF analysis and brain imaging features; viral etiology was considered when CSF had slightly elevated protein, low normal blood sugar and moderately elevated lymphocyte count. Bacterial cultures, gramstain and India ink stain were negative in these patients.

Among 8 patients, microbiological confirmation was possible in only 2 patients (case 6 & 19) ; These 2 patients presented with headache, fever and altered sensorium; One patient (case 6) had left temporal and right insular cortex hyperintensity, strongly suggestive of herpes simplex encephalitis; CSF HSV PCR was positive. Another patient had right temporal hyperintensity in MRI and positive HSV PCR in CSF. Both these patients recovered well with 2 weeks course of Inj. Acyclovir (30mg/kg/day).

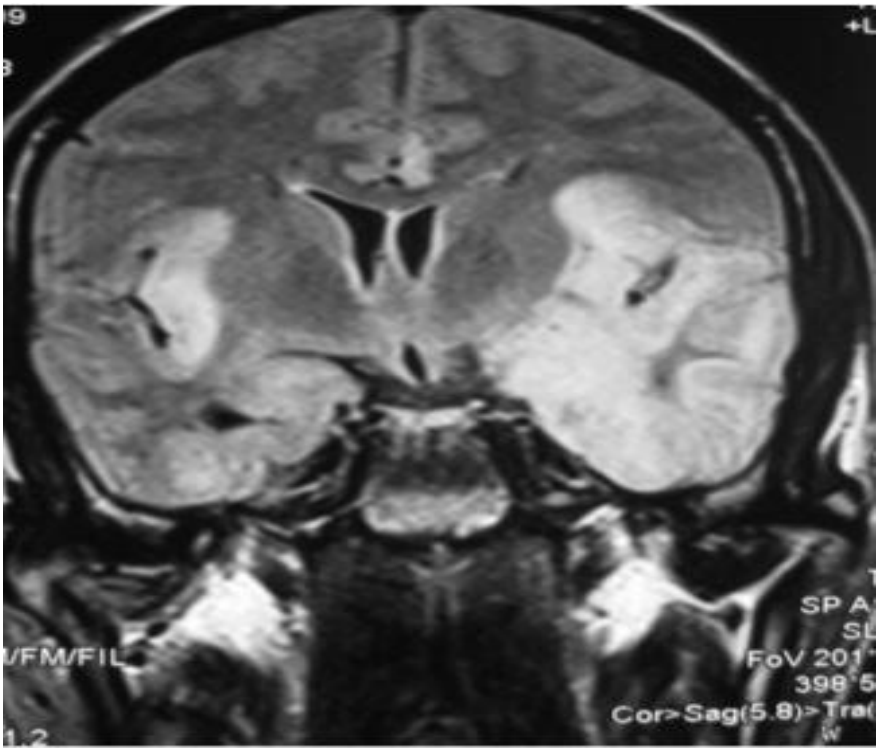
For the remaining patients HSV PCR was negative. All 6 patients recovered completely and were asymptomatic during follow up.

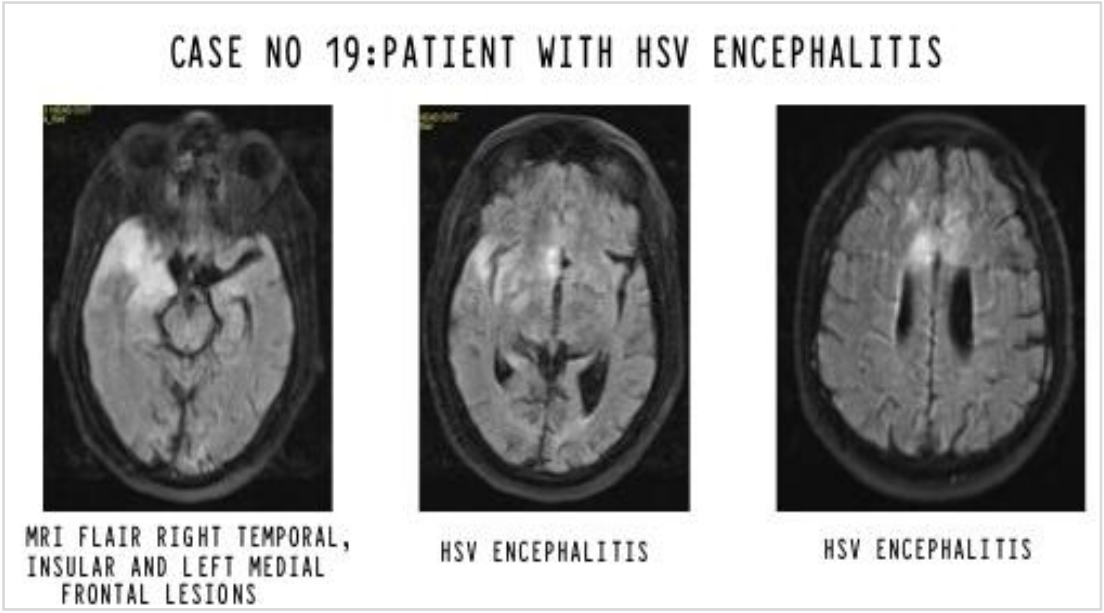
In many cases of presumed viral encephalitis (32%-75%), the responsible organism could not be identified, despite detailed diagnostic testing. In the California Encephalitis Project, 334 patients with encephalitis were studied from 1998 – 2000. Etiological organism was not identified in 208 of 334 patients (62%), despite extensive testing and evaluation.[43]

In a study of 1570 cases over a 7 years period, a confirmed or probable organism was identified for only 16% of cases of encephalitis. Of the confirmed or probable cases, 69% were viral, 20% were bacterial, 7% were prion related, 3% were parasitic and 1% were fungal[44]. No symptoms and signs were specific for viral meningoencephalitis; Negative CSF bacterial culture does not directly point towards viral meningoencephalitis.

Tuberculous meningitis can mimic a viral meningitis, especially when the presentation is acute. Some patients who were treated as viral meningitis came back to the hospital, with tuberculous meningitis(outside the study). Both fungal and tuberculous meningitis can have lymphocytic pleocytosis in the CSF and can be misdiagnosed as viral meningitis in the initial evaluation. So it is the duty of a treating physician to follow up the patient regularly. In our study, though we are unable to isolate the organisms in 6 out of 8 patients with presumed viral meningo encephalitis, we were able to rule out tuberculous or fungal etiology in these patients. Because, these patients recovered well without specific antibiotics, antituberculous and antifungal therapy and they were totally asymptomatic during follow up which confirmed the diagnosis of probable viral etiology.

CASE NO 6: HERPES SIMPLEX ENCEPHALITIS – MRI T2W SHOWS LEFT TEMPORAL AND RIGHT INSULAR HYPERINTENSITY



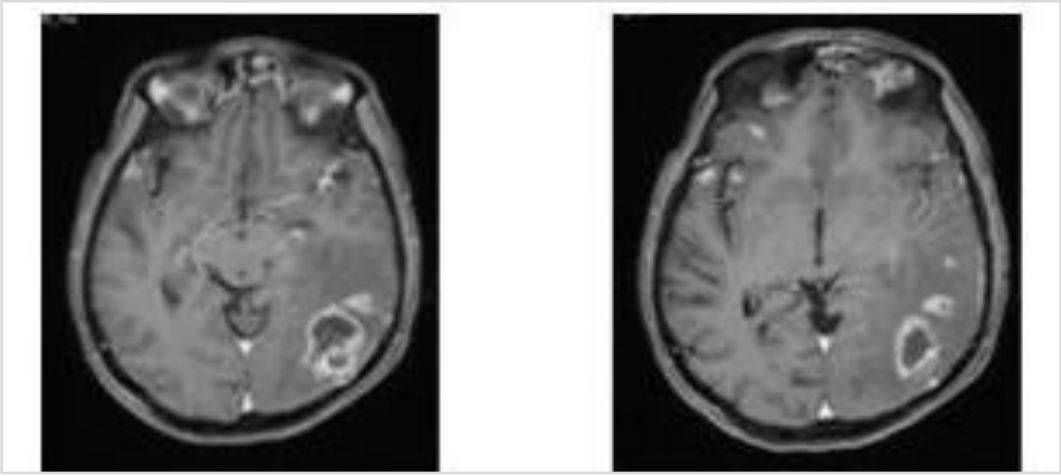


Other causes of acute meningo encephalitis in this study:

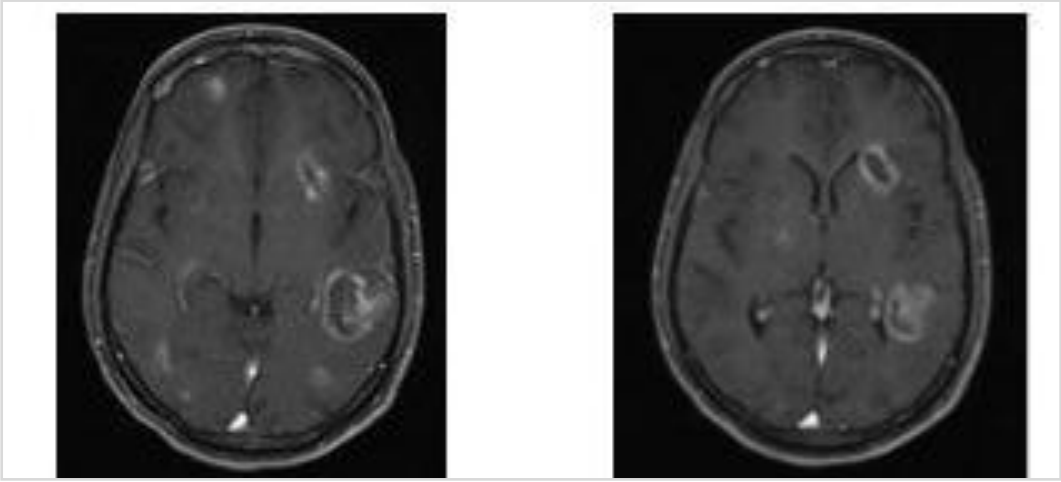
Although commonly tuberculous and cryptococcal meningitis presents with subacute courses, 4 patients of tuberculous meningitis and 1patient of cryptococcal meningitis presented with acute onset illness.

2 patients presented with CNS toxoplasmosis and these patients are found to be HIV infected patients and they presented with hemiparesis and serology for toxoplasma IgG was positive in these patients, both the patients recovered well with appropriate treatment.

CASE NO 21: CEREBRAL TOXOPLASMOSIS



CASE NO 35: CEREBRAL TOXOPLASMOSIS



Subacute Meningitis

Among 50 patients, 23 patients had subacute onset illness. Of these 21 patients were diagnosed as tuberculous meningitis, one patient had cryptococcal meningitis and one patient had aspergillus meningitis.

According to the literature, common cause of subacute meningitis include tuberculous and fungal meningitis. In this study also we have found similar distribution.

Tuberculous Meningitis:

Establishing the diagnosis of tuberculosis etiology is challenging in patients with meningitis. Conventional TB culture method will take long time to give results.

CSF Ziehl neelsen staining is poorly sensitive to show the acid fast bacilli. So, tuberculous meningitis is often diagnosed on the basis of clinical, CSF findings and radiological correlation. In this study, diagnosis of tuberculous meningitis was suspected in patients who presented with subacute onset fever, headache and altered sensorium. Elevated protein and lymphocytic pleocytosis in CSF, presence of basal meningeal exudates, presence of tuberculoma, hydrocephalus and typical distribution of vasculitic infarcts in the capsuloganglionic region in brain imaging suggested the diagnosis of probable tuberculous meningitis in these patients.

Diagnostic features for tuberculous Meningitis45

Clinical

- Fever and headache (for more than 14 days)
- Vomiting
- Altered sensorium or focal neurological deficits

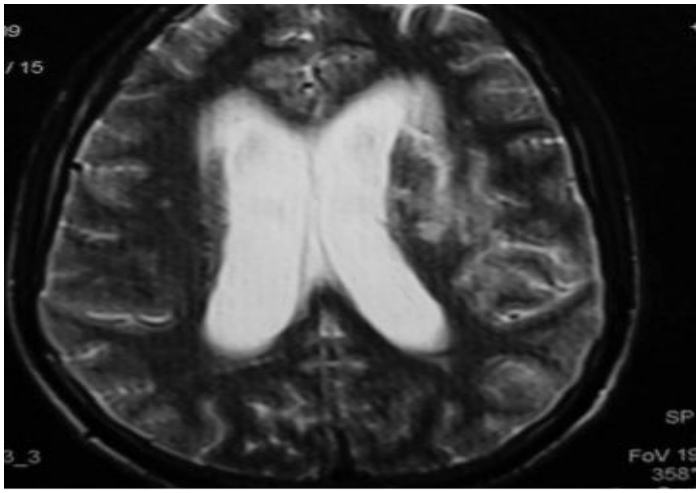
CSF

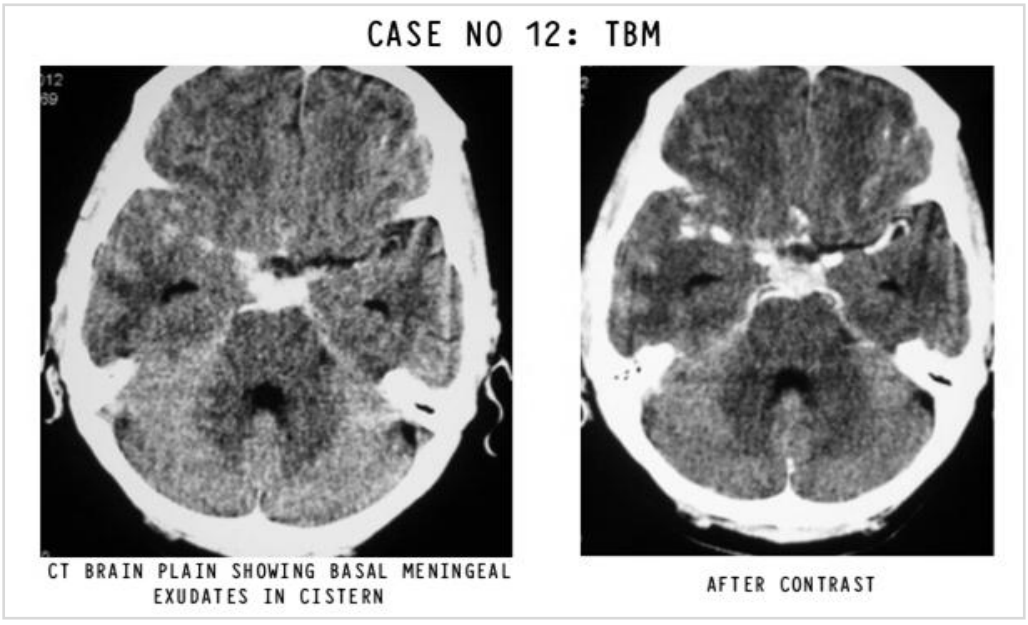
- Pleocytosis (more than 20 cells, of which more than 60% are lymphocytes)
- Increased protein (more than 100mg/dl)
- Low sugar (less than 60% of corresponding blood sugar)
- Low chloride levels especially in HIV infection
- India ink stain and microscopy for malignant cells should be negative.

Imaging

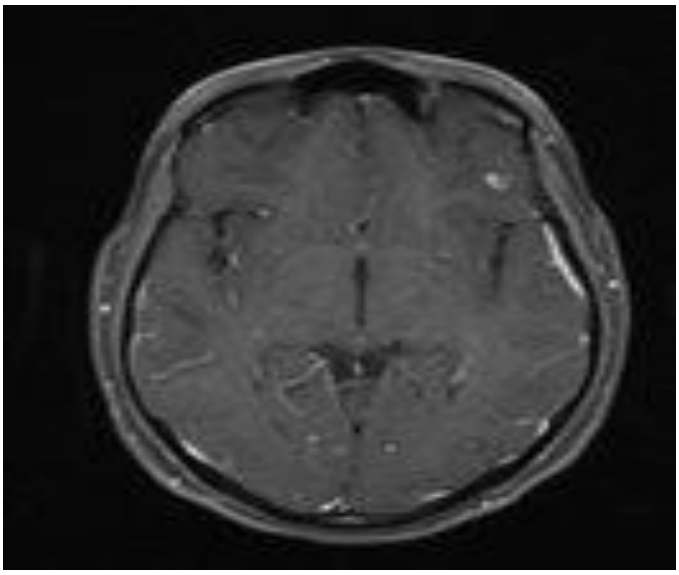
- Exudates in basal cisterns or sylvian fissure, hydrocephalus
- Basal ganglionic infarcts
- Gyral enhancement
- Tuberculoma formation

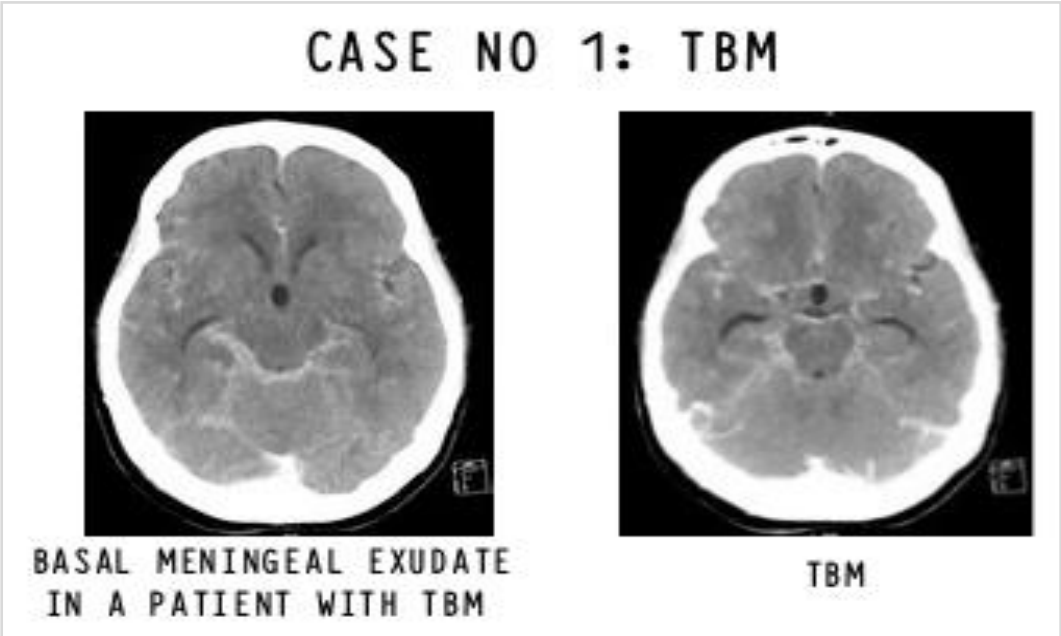
CASE NO 5: TBM WITH HYDROCEPHALUS –MRI T2W





CASE NO 18: TBM WITH LEFT FRONTAL TUBERCULOMA IN CONTRAST MRI





Among 50 patients, 29 patients were diagnosed as tuberculous meningitis. 21 patients had subacute presentation, 4 patients had acute presentation and 4 patient had chronic presentation.

Headache was present in 23 patients; 24 patients had fever and only 17 patients had altered sensorium in the course of illness; Only 12 patients (41%) had neck stiffness; Remaining 59% of patients did not have neck stiffness; Our study indicates that neck stiffness is not a sensitive sign to diagnose tuberculous meningitis.

CSF analysis revealed elevated protein ranging from 100 to 600mg/dl. All patient had elevated cell count, predominantly lymphocytes in the CSF. Total cell count in CSF ranged from 100-1400 cell/$mm^{3.}$ No patients had positive AFB on Ziehl Neelsen stain of CSF. CSF TB PCR was positive in only 2 patients.

A Vietnamese study compared clinical outcome of 143 adults with TBM and 108 with presumed pyogenic meningitis. The authors of the study developed a diagnostic rule based on five variables - age, duration of symptoms, blood white blood cell count, CSF white blood cell count and percentage of neutrophils in the CSF. The diagnostic rule had a sensitivity of 86% and specificity of 79% (Thwaites et al 2002). Hence a high index of clinical suspicion is required diagnosing TBM.

In our study 15 patients (52%) had basal meningeal exudates in brain imaging (MRI Brain). Few patients underwent only CT scan which revealed basal meningeal enhancement. Hydrocephalus was present in 5 patients. Only 2 patients had significantly larger hydrocephalus, progressively increasing in size and underwent VP shunt.

With repeated sequential examination of CSF, kennedy and fallon reported tubercle bacilli in 87% of patients. In their study, AFB were visible in stained CSF sediments in 37% patients during initial examinations, but the yield was 87% when the CSF from four serial spinal taps was examined[46]. In another study bacteriological diagnosis was made in 107 of 132 adults in clinically suspected TBM. To increase the protein yield, a centrifuged sediment of more than 10 ml of CSF should be used for acid fast staining and 200-500 high power fields should be examined of each specimen for atleast 30 minutes, preferably by more than one observer. Serial CSF examination and examination of ventricular CSF will increase the yield further.[47]

The sensitivity of CSF PCR testing was only 60% in patients classified as having definite or probable TM.[48] In another meta analysis of PCR assay in TBM, the sensitivity was 56% and specificity was 98%.[49]

In two large community based series, hydrocephalus was seen in approximately 75% of patients, basilar meningeal enhancement in 38%, cerebral infarcts in 15% -30% and tuberculomas in 5-10%.[50,51]

Early diagnosis of TBM is crucial, because early initiation of treatment will prevent disability and irreversible complications. Empirical antituberculous therapy should be started in the setting of compatible clinical, epidemiological and laboratory findings. With early appropriate antituberculous therapy and steroids, all patients in this study recovered well without neurological deficits.

Cryptococcal Meningitis

In this study 2 patients had cryptococcal meningitis ; one patient had HIV infection and another one had no HIV infection.

The patient without HIV infection, a diabetic, presented atypically with tiredness, lethargy, dullness, apathy, anorexia and intermittent confusion of 1 week duration; Due to lack of headache and fever possibility of CNS infection was not considered in the initial few days. MRI brain revealed small basal ganglionic infarct. CSF analysis surprisingly revealed positive cryptococcal antigen in high titres. India ink stain was positive and he was started on amphotericin B and high dose IV fluconazole. Despite appropriate drug therapy, he rapidly deteriorated, comatosed and expired.

The patient with HIV infection and cryptococcal meningitis recovered well with amphotericin.

Aspergillus Meningitis

In this study, we came across an interesting and rare case of aspergillus meningitis. This 53 years old male developed right trigeminal neuropathy in 2011. MRI brain showed small T2 hyperintense extra axial lesion in the right middle cranial fossa medial to right temporal lobe. The lesion was surgically removed and histopathology revealed aspergilloma. He continued antifungal therapy for 6months (Inj. Amphotericin B) and discontinued. In 2013 he developed recurrence of lesion in the similar site. He was started on oral voriconazole and the lesion disappeared with voriconazole. He discontinued the tablet 1 year later. In Jan 2015, he presented with one month duration of daily, severe and persistent headache. He had mild neck stiffness and no neurological deficits. CT brain plain and contrast revealed hydrocephalus with dilatation of all 4 ventricles and there was no brain parenchyma or extra axial lesion. Due to the past history of intra cranial aspergilloma, possibility of aspergillus meningitis was strongly considered, CSF analysis showed elevated protein and elevated lymphocyte count. CSF PCR for aspergillus was positive. CSF TB PCR was negative and cryptococal antigen was negative. He was diagnosed as aspergillus meningitis and started on IV voriconazole. As the hydrocephalus did not reduce and he had persistent severe headache, VP shunt was done. He is on regular oral voriconazole to

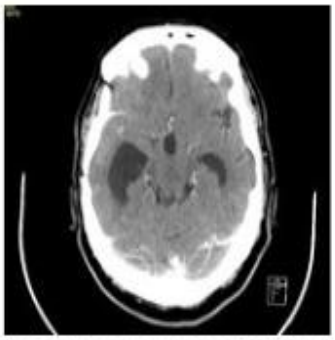
prevent further relapse and he is asymptomatic at present. Aspergillus Meningitis is a rare entity and there are only few reported cases in the world literature. Aspergillus meningitis has been reported to be co-existent with active granulomatous or rhinocerebral lesion. Our patient is unique that he developed meningitis without co-existent intracranial aspergilloma.

CASE NO 30: ASPERGILLUS MENINGITIS

CASE 30: 2011 MRI BRAIN

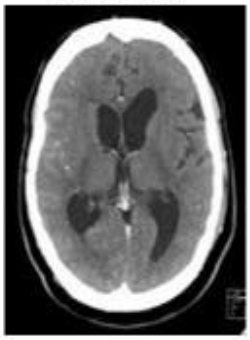
RIGHT TEMPORAL ARPERGILLOMA

CASE 30: ASPERGILLUS MENINGITIS- 2015



CT SHOWING HYDROCEPHALUS

CASE 30: ASPERGILLUS MENINGITIS



OUTCOME

In this study, outcome was assessed by detailed neurological assessment at the end of one month. Scoring was done with Barthel index.

Among 50 patients, 47 patients recovered completely without neurological deficits. All these 47 patients had barthel Index 100, at the end of one month.

One patient (case 22) with pneumococcal Meningitis had extensive vasculitic brain and brain stem infarcts. He had severe neurological deficits requiring help for all daily activities at the end of one month. At the end of one month, his Barthel Index was 0.

A patient with pneumoncoccal meningitis (case 4) and a patient with cryptococcal meningitis (case 23) had rapidly progressive fulminant course and they succumb to the illness at the end of 1 week despite appropriate drug treatment.

ACUTE PYOGENIC MENINGITIS PATIENTS IN THE STUDY

S. No	Case No.	Age / Sex	GCS	Protein	Sugar	Cell count (TC)	Cell count DC (P/N)	CSF rhinorrhea	Infarcts
1	2	31/M	13	120	40	220	58/42	-	-
2	4	35/M	3	150	40	1200	99/1	-	+++
3	10	43/F	13	138	94	15000	94/6	+	-
4	11	26/M	14	387	5	15000	98/2	-	-
5	22	27/M	8	543	0.5	550	95/5	+	+++
6	40	26/M	8	741	0.8	8500	89/11	+	-
7	43	26/M	13	230	75	7500	75/25	+	-
8	50	54/F	15	130	30	250	60/40	-	-

CONCLUSION

1. In this study, most of the patients with meningoencephalitis were males and young adults.

2. Surprisingly, tuberculous meningitis was the most common overall cause in this study. This observation is in contrast to the Western literature. Viral etiology in the most common one in western population.

3. Both viral meningo encephalitis and pyogenic meningitis constituted most of the cases of acute Meningoencephalitis.

4. Tuberculous meningitis was the most common cause in patient with subacute meningitis. Diagnosis of tuberculous meningitis was challenging; clinical presentation, CSF studies, and brain imaging features helped to make a diagnosis of tuberculous meningitis. All patients with chronic presentation (> 4 weeks) had tuberculous meningitis.

5. We came across atypical presentation of cryptococcal meningitis in a non HIV patient and cases of cerebral toxoplasmosis in patients with HIV infection

6. In this study, we are reporting an interesting case of aspergillus Meningitis which is a very rare entity especially without co-existent aspergilloma.

7. A patient with pneumococcal meningitis and another one with cryptococcal meningitis had fulminant course and died despite appropriate drug therapy. 47 patients recovered well without neurological deficits.

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QUESTIONNAIRE (PROFORMA)

Name : _____

Age : _____

Sex : Male ☐ Female ☐

Occupation: _____

Address:

_____

Chief complaints :

S.NO	COMPLAINTS	PRESENT	ABSENT	DURATION
1.	Fever			
2.	Headache			
3.	Nausea			
4.	Vomiting			
5.	Altered mental status			
6.	History of personality and/or behavioural changes			
7.	History of lethargy			
8.	History of irritability			
9.	History of seizures: focal/GTCS/focal with secondary generalization/status epilepticus			
10.	History of cranial nerve involvement			
11.	History of motor/sensory deficit			
12.	History of presence of rash			
13.	History of otitis/sinusitis			
14.	History suggestive of pneumonia			
15.	History of constitutional symptoms			
16.	History of bleeding manifestations			
17.	Historty suggestive of other systemic compromise(renal/liver/lungs)			

History of Present illness and Past history:

History of recent hospitalization :

History of recent travel :

History of recent vaccination :

History of similar illness in the past:

Medication History :

History of surgical operation :

History of chicken pox in the past :

History of diabetes :

History of tuberculosis :

Family history of tuberculosis contacts:

History of smoking/alcohol :

Insect contact/animal contact :

Marietal history/sexual history :

General examination:

Glasgow coma scale at the admission:

Vitals :

Temperature :

Heart rate :

Blood pressure :

Respiratory rate :

Arterial oxygen saturation :

Neurological examination:

Speech :

Fundus examination :

Cranial nerve examination :

Motor system examination :

Neck stiffness :

Other System examination:

Investigations:
Complete blood picture
Urine routine
Random blood sugar
ECG
Chest X Ray
Renal and liver function tests
Blood Culture and Urine culture
HIV
CSF glucose, protein, ADA
CSF white cell count (TC/DC),cytology
CSF gram stain for Bacteria /AFB stain for Tuberculosis
CSF for Bacterial Culture
CSF automated culture for AFB
CSF India ink for Cryptococcus/cryptococcal antigen test
Neuroimaging(CT brain - plain/contrast / MRI brain - plain/contrast)

If needed :
CSF for Fungal culture
EEG
CSF PCR(HSV/MTB), toxoplasma IgG

Outcome:

BARTHEL INDEX (score) at the end of one month:

ABBREVIATIONS

CSF	-	cerebrospinal fluid
Z.N STAIN	-	zeihl neelsen stain
AFB	-	acid fast bacteria
LP	-	lumbar puncture
CT	-	Computed tomography
MRI	-	Magnetic resonance imaging
BS	-	fasting blood glucose
CNS	-	Central nervous system
HIV	-	human immunodeficiency virus
AIDS	-	acquired immune deficiency syndrome
ICP	-	intracranial pressure
ECG	-	Electrocardiogram
ECHO	-	Echocardiography
PCR	-	polymerase chain reaction
EEG	-	electroencephalogram
HSV	-	herpes simplex virus

ELISA	-	enzyme linked immunosorbent assay
VDRL	-	venereal disease research laboratory
FTA-ABS	-	fluorescent treponemal antibody absorption test
PPD	-	purified protein derivative test
LCMV	-	lymphocytic choriomeningitis
MIC	-	minimum inhibitory concentration
MTB/TB	-	mycobacterium tuberculosis
GCS	-	glasgow coma scale
TBM/TM	-	tuberculous meningitis
APM	-	acute pyogenic meningitis
VME	-	viral meningoencephalitis
CM	-	cryptococcal meningitis
CT	-	cerebral toxoplasmosis
AM	-	aspergillus meningitis
VP SHUNT	-	ventriculoperitoneal shunt
TC	-	total WBC count
DC(P/L)	-	differential count(polymorphs/lymphocytes)

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I **Dr. Divya peddireddy** carrying out a study on the topic :

Etilogical, clinical profile and outcome in adults with meningitis and meningoencephalitis.

as part of my / our research project being carried out under the aegis of the Department of Medicine :

(*Applicable to students only*): My research guide is **: Dr.Jayachandran.K , Dr.R.Balakrishnan**

The justification for this study is:

There are no studies done till now showing the clinical profile, etiological profile and outcome in patients with meningitis and meningoencephalitis.There are some studies done in children but not in adults.

As there are fewer developments in therapies for viral meningitis and there remain no effective therapies for most pathogens. Thus this study emphasis the importance of early diagnosis so that prompt management is given at appropriate time and distinguishing etiologies helps in terms of both reducing antibiotic usage and hospital bed occupancy and reassuring contacts of cases and health care staff of a non-bacterial cause.

The objectives of this study are:

To establish the cause and identify the clinical differences between causes and outcome in adults with meningitis and meningoencephalitis in a tertiary care hospital

Sample size: 50 adults of age more than 18 years.

Study volunteers / participants are (specify population group & age group): All adults more than 18 years with meningitis / meningoencephalitis of various etiologies admitted in general

medicine and neurology departments of PSGIMSR during the period of July 2014 to June 2015

Location: General medicine and neurology departments of PSGIMSR.

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview (specify approximate duration): 20 minutes. Questionnaire will be used to collect data on patients history, signs on admission, laboratory findings ,clinical course, treatment and outcome.
Data collected will be stored for a period of FIVE years. We will / will not use the data as part of another study.

Health education sessions: NOT APPLICABLE

Clinical examination (Specify details and purpose): General examination and systemic examination including neurological examination

Blood sample collection: NOT APPLICABLE

Medication: NOT APPLICABLE

Final interview:. Follow-up of patients at 1 month after discharge from hospital outcome was scored according to Glasgow outcome scale

If **photograph** is taken, purpose: NOT APPLICABLE

Benefits from this study :

1. **The study will establish the cause of meningitis and meningoencephalitis.**
2. **To measure the outcome in terms of neurological complications.**
3. **The study helps in terms of reducing antibiotic usage and prompt management**

Risks involved by participating in this study: No Risk

How the **results** will be used: FOR DISSERTATION AND PUBLICATION.

If you are uncomfortable in answering any of our questions during the course of the interview , **you have the right to withdraw from the study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to

indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).
Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: 8754452685

Contact number of Ethics Committee Office: 0422 2570170 Extn.: 5818

LIST OF FIGURES

LIST OF TABLES

MASTER CHART 1:

Case no	Age	Sex	headache	fever	seizures	vomiting	altered mental status	csf rhinorrhea	hemiparesis	speech disturbances	cranial nerve palsy	Duration	neck stiffness	Pappiledema	GCS
1	24	M	Y	Y	3	Y	N	N	N	N	N	2	N	N	2
2	30	M	y	y	3	Y	y	N	y	Y	N	1	N	N	2
3	59	F	N	Y	3	Y	Y	N	N	N	N	1	N	N	2
4	40	M	Y	Y	3	Y	Y	N	N	N	N	1	N	N	1
5	40	M	Y	Y	3	N	N	N	N	N	N	3	N	N	2
6	40	F	Y	Y	3	Y	Y	N	N	N	N	1	Y	N	2
7	55	F	Y	Y	3	N	N	N	N	N	N	2	N	Y	2
8	28	M	Y	Y	3	N	N	N	N	N	N	1	N	N	2
9	36	M	Y	Y	3	Y	N	N	N	N	N	1	N	N	2
10	43	F	Y	Y	3	Y	Y	Y	N	N	N	1	Y	N	2
11	26	M	N	Y	1	N	Y	N	N	N	N	1	Y	N	2
12	52	F	N	Y	3	N	Y	N	N	N	N	2	N	N	2
13	86	M	N	Y	3	N	Y	N	N	N	N	2	Y	N	2
14	18	F	Y	Y	1	Y	N	N	N	N	N	2	N	N	2
15	58	F	N	Y	3	N	Y	N	N	N	N	2	N	N	2
16	51	F	N	Y	3	Y	N	N	N	N	N	3	N	N	2
17	31	M	Y	Y	3	Y	Y	N	N	N	N	2	N	N	2
18	25	F	Y	N	1	N	Y	N	N	Y	Y	2	N	N	1
19	22	M	Y	Y	3	N	Y	N	N	N	N	1	N	N	2
20	49	M	Y	Y	3	N	Y	N	N	N	N	2	N	N	2
21	60	F	N	N	3	N	N	N	Y	N	N	1	N	N	2
22	27	M	Y	Y	3	Y	Y	Y	Y	N	Y	1	Y	N	1
23	58	M	N	N	3	Y	Y	N	N	N	N	1	N	N	1
24	25	M	Y	N	3	N	Y	N	N	N	N	1	N	N	2
25	52	M	Y	Y	3	Y	Y	N	N	N	N	2	Y	N	2

Case no	Age	Sex	headache	fever	seizures	vomiting	altered mental status	csf rhinorrhea	hemiparesis	speech disturbances	cranial nerve palsy	duration	neck stiffness	Pappiledema	GCS
26	47	M	Y	Y	3	N	N	N	N	N	N	1	N	N	2
27	31	M	Y	Y	3	N	Y	N	N	N	N	1	Y	N	2
28	34	M	Y	Y	3	Y	Y	N	N	N	N	1	Y	N	2
29	64	M	N	N	3	N	Y	N	N	N	Y	1	N	N	1
30	50	M	Y	N	3	Y	N	N	N	N	N	2	N	N	2
31	18	F	Y	Y	3	Y	N	N	N	N	N	2	N	Y	2
32	19	M	Y	Y	3	Y	N	N	N	N	N	1	Y	N	2
33	40	M	Y	Y	3	N	N	N	N	N	N	2	Y	N	2
34	35	M	Y	Y	3	N	N	N	N	N	N	2	Y	N	2
35	46	M	N	N	3	N	Y	N	Y	N	N	1	Y	N	2
36	25	M	Y	Y	3	Y	Y	N	N	N	N	2	Y	N	2
37	44	F	Y	Y	3	N	Y	N	N	N	N	2	Y	N	2
38	40	M	Y	Y	3	N	y	N	N	N	N	2	Y	N	1
39	50	M	Y	N	3	N	y	N	N	N	N	3	Y	N	1
40	26	M	N	Y	1	Y	y	Y	N	N	N	1	N	N	1
41	19	M	Y	Y	2	Y	Y	N	N	N	N	2	Y	N	1
42	43	F	Y	N	3	N	N	N	N	N	N	3	N	N	2
43	26	M	Y	Y	1	N	Y	Y	N	N	N	1	Y	N	2
44	38	M	Y	Y	3	Y	N	N	N	N	N	2	N	Y	2
45	45	F	N	Y	3	N	N	N	N	N	N	2	N	N	2
46	42	M	Y	Y	3	N	Y	N	N	N	N	2	Y	N	2
47	20	F	Y	Y	3	Y	N	N	N	N	Y	2	Y	Y	2
48	22	F	Y	Y	3	N	Y	N	N	N	N	2	Y	Y	1
49	42	M	N	Y	3	Y	Y	N	N	N	N	1	Y	N	2
50	54	F	Y	Y	3	Y	N	n	N	N	N	1	N	N	2

MASTER CHART 2:

Case no	HIV	CSF protein	CSF glucose	CSF TC	CSF DC	Organism	MRI-normal	MRI-meningeal enhancement	hydrocephalus	granuloma	vasculitic infarcts	VP shunt	DIAGNOSIS	Outcome
1	N	1	2	2	1	0	N	Y	N	N	N	N	3	0
2	N	2	1	1	2	0	Y	N	N	N	N	N	1	0
3	N	1	1	1	1	0	N	Y	N	N	N	N	2	0
4	N	2	1	2	2	1	N	Y	N	N	Y	N	1	2
5	N	1	1	1	1	0	N	N	Y	N	N	Y	3	0
6	N	1	3	1	1	2	N	Y	N	N	N	N	2	0
7	N	1	1	1	1	0	Y	N	N	N	N	N	3	0
8	N	2	3	1	1	0	Y	N	N	N	N	N	2	0
9	N	1	3	1	1	0	Y	N	N	N	N	N	2	0
10	Y	2	1	2	2	0	Y	N	N	N	N	N	1	0
11	N	2	2	2	2	1	Y	N	N	N	N	N	1	0
12	N	2	2	1	1	0	N	Y	N	N	N	N	3	0
13	N	2	3	1	1	1	Y	N	N	N	N	N	3	0
14	N	1	1	1	1	0	N	Y	N	N	N	N	3	0
15	N	2	2	1	1	0	Y	N	N	N	N	N	3	0
16	N	2	1	1	1	0	N	Y	Y	N	N	N	3	0
17	N	2	2	1	1	0	N	Y	N	N	N	N	3	0
18	N	2	2	1	1	0	N	Y	N	Y	N	N	3	0
19	N	1	3	1	1	2	N	Y	N	N	N	N	2	0
20	N	2	1	1	1	0	Y	N	N	N	N	N	3	0
21	Y	1	3	1	1	5	N	Y	N	Y	N	N	5	0
22	N	2	2	1	2	1	N	Y	N	N	Y	N	1	1
23	N	1	2	1	1	4	N	Y	N	N	Y	N	4	2
24	N	2	2	1	1	0	N	Y	N	Y	N	N	3	0
25	Y	2	2	1	1	3	Y	N	N	N	N	N	3	0

Case no	HIV	CSF protein	CSF glucose	CSF TC	CSF DC	organism	MRI-normal	MRI-meningeal enhancement	hydrocephalus	granuloma	vasculitic infarcts	VP shunt	DIAGNOSIS	outcome
26	N	2	2	1	1	3	Y	N	N	N	N	N	3	0
27	N	1	1	1	1	0	Y	N	N	N	N	N	3	0
28	N	1	3	1	1	0	Y	N	N	N	N	N	2	0
29	N	2	1	1	1	0	N	Y	N	N	Y	N	3	0
30	N	2	1	1	1	6	N	N	Y	N	N	Y	4	0
31	N	1	1	1	1	0	Y	N	N	N	N	N	3	0
32	N	1	3	1	1	0	Y	N	N	N	N	N	2	0
33	Y	1	1	1	1	4	N	Y	N	N	N	N	4	0
34	N	1	2	1	1	0	Y	N	N	N	N	N	3	0
35	y	2	1	1	1	5	N	Y	N	Y	N	N	5	0
36	N	2	2	1	1	0	N	Y	N	N	N	N	3	0
37	N	2	2	1	1	0	N	Y	N	N	N	N	3	0
38	N	2	2	1	1	0	Y	N	N	N	N	N	3	0
39	Y	2	2	1	1	0	N	Y	Y	Y	N	N	3	0
40	N	2	2	2	2	1	N	Y	N	N	N	N	1	0
41	N	1	1	2	1	0	N	Y	N	N	N	N	3	0
42	N	1	1	1	1	0	Y	N	N	N	N	N	3	0
43	N	2	1	2	2	0	Y	N	N	N	N	N	1	0
44	N	1	1	1	1	0	Y	N	N	N	N	N	3	0
45	N	1	1	1	1	0	Y	N	N	N	N	N	3	0
46	N	1	1	1	1	0	N	Y	Y	N	Y	N	3	0
47	N	1	1	1	1	0	N	Y	N	N	N	N	3	0
48	N	1	1	1	1	0	N	Y	Y	N	N	Y	3	0
49	N	2	2	1	1	0	Y	N	N	N	N	N	2	0
50	N	2	2	1	2	0	Y	N	N	N	N	N	1	0

MASTER KEY CHART 1:

Y-YES

N-NO

SEX-

M- MALE

F- FEMALE

SEIZURE-

GTCS-1

FOCAL-2

no-3

DURATION-

ACUTE 1

SUBACTE 2

CHRONIC 3

GCS-

LESS THAN 10-1

MORE THAN 10-2

MASTER KEY CHART 2:

CSF PROTEIN-

1-increased

2-markedincrease(>100)mg/dl)

CSF GLUCOSE-

1-low glucose

2-markedly low(40mg/dl)

3-normal

CSF TC-

1-pleocytosis

2-marked pleocytosis (>1000cells/cumm

CSF DC-

1-lymphocytic

2-neutrophilic

MASTER KEY CHART 2:

Organism-

BACTERIAL 1

VIRAL 2

TUBERCOLOSIS 3

CRYPTOCCUS 4

TOXOPLASMA 5

ASPERGILLUS 6

NIL -0

DIAGNOSIS-

1-acute pyogenic meningitis

2-VIRAL MENINGOENCEPHALITIS

3-tuberculous meningitis

4-FUNGAL MENINGITIS

5-CNS TOXOPLASMASMOSIS

MASTER KEY CHART 2:

Outcome-

BARTHEL INDEX 100- 0

BARTHEL INDEX 0- 1

DEATH -2

FUNCTIONAL EVALUATION: THE BARTHEL INDEX

A simple index of independence useful in scoring improvement in the rehabilitation of the chronically ill

BARTHEL INDEX

	With Help	*Independent*
1. Feeding (if food needs to be cut up = help)	5	10
2. Moving from wheelchair to bed and return (includes sitting up in bed)	5-10	15
3. Personal toilet (wash face, comb hair, shave, clean teeth)	0	5
4. Getting on and off toilet (handling clothes, wipe, flush)	5	10
5. Bathing self	0	5
6. Walking on level surface (or if unable to walk, propel wheelchair) *score only if unable to walk	0*	5*
7. Ascend and descend stairs	5	10
8. Dressing (includes tying shoes, fastening fasteners)	5	10
9. Controlling bowels	5	10
10. Controlling bladder	5	10

A patient scoring 100 BI is continent, feeds himself, dresses himself, gets up out of bed and chairs, bathes himself,walks at least a block, and can ascend and descend stairs. This does not mean that he is able to live alone: he may not be able

to cook, keep house, and meet the public, but he is able to get along without attendant care.

DEFINITION AND DISCUSSION OF SCORING

1. Feeding

10 = Independent. The patient can feed himself a meal from a tray or table when someone puts the food within his reach. He must put on an assistive device if this is needed, cut up the food, use salt and pepper, spread butter,etc. He must accomplish this in a reasonable time.

5 = Some help is necessary (with cutting up food, etc., as listed above).

2. Moving from wheelchair to bed and return

15 = Independent in all phases of this activity. Patient can safely approach the bed in his wheelchair, lock brakes, lift footrests, move safely to bed, lie down, come to a sitting position on the side of the bed, change the position of the wheelchair, if necessary, to transfer back into it safely, and return to the wheelchair.

10 = Either some minimal help is needed in some step of this activity or the patient needs to be reminded or supervised for safety of one or more parts of this activity.

5 = Patient can come to a sitting position without the help of a second person but needs to be lifted out of bed, or if he transfers with a great deal of help.

3. Doing personal toilet

5 = Patient can wash hands and face, comb hair, clean teeth, and shave. He may use any kind of razor but must put in blade or plug in razor without help as well as get it from drawer or cabinet. Female patients must put on own makeup, if used, but need not braid or style hair.

4. Getting on and off toilet

10 = Patient is able to get on and off toilet, fasten and unfasten clothes, prevent soiling of clothes, and use toilet paper without help. He may use a wall bar or other stable object for support if needed. If it is necessary to use a bed pan instead of a toilet, he must be able to place it on a chair, empty it, and clean it. Patient needs help because
of imbalance or in handling clothes or in using toilet paper.

5. Bathing self

5 = Patient may use a bath tub, a shower, or take a complete sponge bath. He must be able to do all the steps involved in whichever method is employed without another person being present.

6. Walking on a level surface

15 = Patient can walk at least 50 yards without help or supervision. He may wear braces or prostheses and use crutches, canes, or a walkerette but not a rolling walker. He must be able to lock and unlock braces if used, assume the standing position and sit down, get the

necessary mechanical aides into position for use, and dispose of them when he sits. (Putting on and taking off braces is scored under dressing.)

10 = Patient needs help or supervision in any of the above but can walk at least 50 yards with a little help.

6a. Propelling a wheelchair

5 = If a patient cannot ambulate but can propel a wheelchair independently. He must be able to go around corners, turn around, maneuver the chair to a table, bed, toilet, etc. He must be able to push a chair at least 50 yards. Do not score this item if the patient gets score for walking.

7. Ascending and descending stairs

10 = Patient is able to go up and down a flight of stairs safely without help or supervision. He may and should use handrails, canes, or crutches when needed. He must be able to carry canes or crutches as he ascends or descends

stairs.

5 = Patient needs help with or supervision of any one of the above items.

8. Dressing and undressing

10 = Patient is able to put on and remove and fasten all clothing, and tie shoe laces (unless it is necessary to use adaptations for this). The activity includes putting on and removing and fastening corset or braces when these are prescribed. Such special clothing

as suspenders, loafer shoes, dresses that open down the front may be used when necessary.

5 = Patient needs help in putting on and removing or fastening any clothing. He must do at least half the work himself. He must accomplish this in a reasonable time.

Women need not be scored on use of a brassiere or girdle unless these are prescribed garments.

9. Continence of bowels

10 = Patient is able to control his bowels and have no accidents. He can use a suppository or take an enema when necessary (as for spinal cord injury patients who have had bowel training).

5 = Patient needs help in using a suppository or taking an enema or has occasional accidents.

10. Controlling bladder

10 = Patient is able to control his bladder day and night. Spinal cord injury patients who wear an external device and leg bag must put them on independently, clean and empty bag, and stay dry day and night.

5 = Patient has occasional accidents or can not wait for the bed pan or get to the toilet in time or needs help with an external device.

A score of 0 is given in all of the above activities when the patient cannot meet the criteria as defined above.